Electronic Supplementary Material (ESI) for Green Chemistry

Supplementary Information

An in-water, on-water domino process for synthesis.

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General Experimental:

All solvents and reagents were used as received from commercial sources. Melting points were determined using a Stanford Research Systems Optimelt automated melting point system and are uncorrected. Infrared spectra were acquired neat on a Bruker Alpha-E ATR spectrometer. UV-vis absorption spectra were recorded on a Varian Cary 50 conc spectrophotometer and absorption maxima are expressed in wavenumbers (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX300 (^{1}H frequencies 300MHz; ^{13}C frequencies 75). ^{1}H chemical shifts are expressed as parts per million (ppm) with residual chloroform (δ 7.26) or residual acetone (δ 2.09) as reference and are reported as chemical shift (δ_H); relative integral; multiplicity (s = singlet, br = broad, d = doublet, t = triplet, dd = doublet of doublets, dt = doublet of triplets, q = quartet, m = multiplet); and coupling constants (*J*) reported in Hz. ^{13}C NMR chemical shifts are expressed as parts per million (ppm) with residual chloroform (δ 77.1) or or residual acetone (δ 30.6) as internal reference and are reported as chemical shift (δ_C); multiplicity (assigned from DEPT experiments). High resolution mass spectra were recorded on a Bruker ApexII Fourier Transform Ion Cyclotron Resonance mass spectrometer with a 7.0 T magnet, fitted with an off-axis Analytical electrospray source. Selected mass spectrometric results were obtained at the Bioanalytical Mass Spectrometry Facility within the Mark Wainwright Analytical Centre of the University of New South Wales. Subsidised access to this facility is gratefully acknowledged.

Experimental section

2-(*N*-Anilino)-5-methylbenzoquinone (2).[1, 2] To a 21 mL screw top vial containing aqueous hydrogen peroxide (30% w/w; 10 mL) was added toluhydroquinone (273 mg, 2.20 mmol), aniline (91 μL, 1.0 mmol) and I_2 (25 mg, 0.1 mmol). The mixture was stirred vigorously overnight, after which a purple solid was evident. The mixture was diluted with aqueous sodium hydrogen carbonate (50 mL) and extracted with dichloromethane (4 × 10 mL). The solvent was removed and the residue was subjected to flash chromatography, eluting with 10% ethyl acetate in hexanes, to give the *title compound* (125 mg, 58%) as a purple solid. mp 145–146 °C (decomp.) (Lit.[3] 150–151 °C); R_f 0.36 (20 % ethyl acetate in hexanes); υ_{max} (solid)/cm^{-1} 3266, 1672, 1644, 1599, 1572, 1513, 1447, 1295; λ_{max} (EtOH) 258 (log ε 4.07), 389 (3.09), 493 nm (3.21); ^{1}H NMR (300 MHz; $CDCl_3$): 7.43–7.16 (6 H, m), 6.58 (1 H, q, *J* 1.5 Hz), 6.18 (1 H, s), 2.10 (3 H, d, *J* 1.5 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) 186.8 (C), 183.9 (C), 149.7 (C), 143.1 (C), 137.6 (C), 129.7 (CH), 129.4 (CH), 125.4 (CH), 122.2 (CH), 101.1 (CH), 16.5 (CH_3); HRMS (ESI) calcd for $C_{13}H_{11}NO_2Na$ (MNa^+) 236.06820, found 236.06797,

and 2-**(*N*-anilino)-6-methylbenzoquinone (7)**[1, 2] (75 mg, 35%) as a purple solid. mp 149–150 °C (decomp.) (Lit.[2] 154–155 °C); R_f 0.24 (20 % ethyl acetate in hexanes); υ_{max} (solid)/cm^{-1} 3317, 1643, 1580, 1524, 1443, 1275; λ_{max} (EtOH) 262 (log ε 4.19), 370 (3.37), 495 nm (3.20); ^{1}H NMR (300 MHz; $CDCl_3$) 7.44–7.04(6 H, m), 6.53 (1 H, dd, *J* 2.4, 1.5 Hz), 6.14 (1 H, d, *J* 2.4 Hz), 2.09 (3 H, d, *J* 1.5 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) 186.9 (C), 184.5 (C), 143.1 (C), 141.3 (C), 137.7 (C), 136.1 (CH), 129.7 (CH), 125.4 (CH), 122.3 (CH), 100.9 (CH), 15.5 (CH_3); HRMS (ESI) calcd for $C_{13}H_{11}NO_2Na$ (MNa^+) 236.06820, found 236.06839.

Murrayaquinone-A (1).[4, 5] A mixture of 2-(*N*-anilino)-5-methylbenzoquinone (2) (38 mg, 0.18 mmol), palladium (II) acetate (46 mg, 0.19 mmol) and cupric acetate (40 mg, 0.20 mmol) in glacial acetic acid (5 mL) was heated under reflux for 48 h with gentle stirring. The mixture was cooled to room temperature and poured onto aqueous sodium hydrogen carbonate (50 mL). Solid sodium hydrogen carbonate was added until the mixture was neutral. The mixture was extracted with ethyl acetate (5 × 30 mL), the solvent was removed and the residue was subjected to flash chromatography, eluting with dichloromethane, to give the *title compound* (37 mg, 98%) as purple needles. mp 236–237 °C (decomp.) (Lit.[2] 237–239 °C); R_f 0.36 (dichloromethane); υ_{max} (solid)/cm^{-1} 3177, 1660, 1632, 1599, 1567, 1404, 1324, 1233; λ_{max} (EtOH) 257 (log ε 4.46), 390 nm (3.64); ^{1}H NMR (300 MHz; $(CD_3)_2CO$ + DMSO-d_6) 12.78 (1 H, br s), 8.12 (1 H, d, *J* 8.1 Hz), 7.60 (1 H, d, *J* 8.4 Hz), 7.44–7.31 (2 H, m), 6.61 (1 H, br q, *J* 1.5 Hz), 2.12 (3 H, d, *J* 1.5 Hz); ^{13}C NMR (75 MHz; $(CD_3)_2CO$ + DMSO-d_6) 184.3 (C), 181.4 (C), 149.4 (C), 139.0 (C), 137.3 (C), 132.9 (CH), 127.4 (CH), 125.1 (C), 124.9 (CH), 123.0 (CH), 117.0 (C), 115.1 (CH), 16.5 (CH_3).

***epi*-Murrayaquinone-A (*epi*-1)**.[2] A mixture of 2-anilino-6-methyl-1,4-benzoquinone (10.6 mg, 0.050 mmol), palladium acetate (13 mg, 0.051 mmol) and cupric acetate (21 mg, 0.10 mmol) were taken up in glacial acetic acid (5 mL). The reaction mixture was stirred under reflux for 48 hours, then poured over saturated $NaHCO_3$ solution (50 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organic phases were dried (Na_2SO_4), the solvent removed and the residue was subjected to flash chromatography on silica, eluting with

dichloromethane to give the *title compound* (10.3 mg, 98%) as a red solid; mp 239 °C (decomp.) (lit. mp 237-239 °C); δ_H (300 MHz; DMSO-d_6) 12.82 (1H, br s, NH), 8.00 (1H, d, ArH), 7.53 (1H, d, ArH), 7.38 (1H, t, ArH), 7.29 (1H, t, ArH), 6.58 (1H, d, ArH), 2.04 (3H, d, CH_3); δ_C (75 MHz; DMSO-d_6) 183.4, 180.2, 144.1, 137.7, 135.8, 134.8, 126.4, 123.8, 123.3, 121.7, 115.6, 113.8, 15.0.

2-(2-Chloroanilino)-5-methyl-1,4-benzoquinone (2a). Toluhydroquinone (240 mg, 1.93 mmol) and 2-chloroaniline (97 μL, 0.92 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 4 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (2 × 25 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give **2a** (48 mg, 21%) as a red solid. mp 102 °C; λ_{max} ($CHCl_3$)/nm 489 (ε 2520), 289 (5360); ν_{max} (solid)/cm^{-1} 3329, 1707, 1671, 1644, 1605, 1585, 1524, 1443, 1359, 1291, 1221, 1175; δ_H (300 MHz; $CDCl_3$) 7.55 (1H, s, NH), 7.50-7.40 (2H, m, ArH), 7.31 (1H, dd, ArH), 7.12 (1H, dd, ArH), 6.61 (1H, d, ArH), 6.15 (1H, s, ArH), 2.10 (3H, s, CH_3); δ_C (50 MHz; $CDCl_3$) 187.0, 183.5, 149.4, 142.4, 134.7, 130.5, 129.7, 127.8, 127.1, 125.9, 122.5, 102.1, 16.5; HRMS (ESI) Found MNa^+ 270.0285. $C_{13}H_{10}ClNO_2Na^+$ requires 270.0292.

and **2-(2-chloroanilino)-6-methyl-1,4-benzoquinone (7a)** (30 mg, 13%) as a red solid. mp 126 °C; λ_{max} ($CHCl_3$)/nm 490 (ε 3960), 289 (6230); ν_{max} (solid)/cm^{-1} 3327, 1645, 1584, 1520, 1441, 1275, 1037 891, 759; δ_H (300 MHz; $CDCl_3$) 7.57 (1H, s, NH), 7.48-7.40 (2H, m, ArH), 7.31 (1H, dd, ArH), 7.12 (1H, dd, ArH), 6.54 (1H, s, ArH), 6.11 (1H, d, ArH), 2.11 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 186.9, 184.2, 142.4, 141.8, 135.8, 134.9, 130.5, 127.8, 127.2, 126.0, 122.6, 102.0, 15.6; HRMS (ESI) Found MNa^+ 270.0292. $C_{13}H_{10}ClNO_2Na^+$ requires 270.0292.

2-(3-Chloroanilino)-5-methyl-1,4-benzoquinone (2b). Toluhydroquinone (249 mg, 2.00 mmol) and 3-chloroaniline (100 μL, 0.95 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 4 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate in hexanes, to give **2b** (36 mg, 15%) as a dark purple solid. mp 173-174 °C; HRMS (APCI) Found: MH^+, 248.0470. $C_{13}H_{11}ClNO_2^+$ requires 248.0473; λ_{max} ($CHCl_3$)/nm 489 (ε 1010), 284 (3250); ν_{max} (solid)/cm^{-1} 3239 (NH), 1642, 1576, 1478, 1420, 1220; δ_H (500 MHz; $CDCl_3$) 7.31 (1H, t, ArH), 7.21 (1H, t, ArH), 7.14 (1H, m, ArH), 7.09 (1H, m, ArH), 6.58 (1H, m, H-6), 6.18 (1H, s, H-3), 2.09 (3H, d, CH_3); δ_C (125 MHz; $CDCl_3$) 186.9, 183.6, 149.7, 142.6, 139.0, 135.5, 130.9, 129.5, 125.4, 122.0, 120.1, 102.0, 16.5; *m/z* (APCI) 250/248 (M^+, 32/100%), 213 (86);

and **2-(3-chloroanilino)-6-methyl-1,4-benzoquinone (7b)** (92 mg, 39%) as a dark purple solid. mp 153.3 °C; HRMS (APCI) Found: MH^+, 248.0470. $C_{13}H_{11}ClNO_2^+$ requires 248.0473; λ_{max} ($CHCl_3$)/nm 489 (ε 1550), 289 (6750); ν_{max} (solid)/cm^{-1} 3326 (NH), 1644 (CO), 1575, 1478, 1262; δ_H (200 MHz; $CDCl_3$) 7.40-7.05 (4H, m, ArH), 6.55 (1H, t, ArH), 6.16 (1H, d, ArH), 2.09 (3H, d, CH_3); δ_C (50 MHz; $CDCl_3$) 187.0, 184.3, 142.7, 141.7, 139.0, 136.0, 135.5, 130.8, 125.5, 122.2, 120.2, 101.8, 15.7; *m/z* (APCI) 250/248 (M^+, 32/100%), 213 (85).

2-(4-Chloroanilino)-5-methyl-1,4-benzoquinone (2c).[2] Toluhydroquinone (212 mg, 1.71 mmol) and 4-chloroaniline (112 mg, 0.88 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 18 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give **2c** (68 mg, 31%) as a dark purple solid. mp 153-165 °C; HRMS (ESI) Found: MNa^+, 270.0295. $C_{13}H_{10}ClNO_2Na^+$ requires 270.0292; λ_{max} ($CHCl_3$)/nm 502 (ε 2920), 288 (6450); ν_{max} (solid)/cm^{-1} 3260, 1676, 1643, 1574, 1492, 1463, 1404, 1352, 1093, 887, 817; δ_H (300 MHz; $CDCl_3$) 7.35 (2H, m, ArH), 7.16 (2H, m, ArH), 6.57 (1H, m), 6.11 (1H, s), 2.10 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 186.9, 183.9, 150.0, 143.0, 136.5, 130.9, 130.1, 129.7, 129.1, 126.8, 123.6, 101.6, 16.7;

and **2-(4-chloroanilino)-6-methyl-1,4-benzoquinone (7c)**[2] (26 mg, 12%) as a dark purple solid. mp 164 °C; (Found: MNa^+, 270.0295. $C_{13}H_{10}ClNO_2Na^+$ requires 270.0292); λ_{max} ($CHCl_3$)/nm 497 (ε 2380), 288 (5470); ν_{max} (solid)/cm^{-1} 3310, 1645, 1596, 1491, 1407, 1340, 1277, 1226, 1186, 1094, 899, 819; δ_H (300 MHz; $CDCl_3$) 7.34 (2H, m, ArH), 7.14 (2H, m, ArH), 6.52 (1H, m), 6.06 (1H, d), 2.08 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 187.0, 184.6, 143.2, 141.8, 136.6, 136.3, 131.0, 130.1, 123.7, 101.5, 15.8.

2-**(2,4,5-trichloroanilino)-5-methyl-1,4-benzoquinone (2d)**. Toluhydroquinone (208 mg, 1.67 mmol) and 2,4,5-trichloroaniline (159 mg, 0.81 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2

was added and the reaction mixture was stirred vigorously for 15 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 25 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 5% ethyl acetate-hexanes, to give **2d** (22 mg, 9%) as a red solid. mp 127-130 °C; HRMS (ESI) Found: MH^+, 315.9689. $C_{13}H_9Cl_3NO_2^+$ requires 315.9693; λ_{max} ($CHCl_3$)/nm 506 (ε 530), 291 (1830); ν_{max} (solid)/cm^{-1} 3309, 2921, 2851, 1669, 1649, 1567, 1492, 1454, 1366, 1268, 1187, 1132, 1080, 882; δ_H (300 MHz; $CDCl_3$) 7.53 (1H, s, ArH), 7.19 (1H, s, ArH), 7.13 (1H, s, ArH), 6.86 (1H, d, ArH), 2.12 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 180.8, 180.3, 146.8, 142.4, 134.2, 134.1, 131.0, 130.7, 129.7, 127.9, 127.6, 88.5, 15.6;

and **2-(2,4,5-trichloroanilino)-6-methyl-1,4-benzoquinone (7d)** (21 mg, 8%) as a red solid. mp 169-171 °C; HRMS (ESI) Found: MH^+, 315.9690. $C_{13}H_9Cl_3NO_2^+$ requires 315.9693; λ_{max} ($CHCl_3$)/nm 504 (ε 470), 290 (1700); ν_{max} (solid)/cm^{-1} 3309, 2923, 2851, 1668, 1646, 1572, 1495, 1455, 1371, 1290, 1222, 1165, 1122, 1076, 880; δ_H (200 MHz; $CDCl_3$) 7.53 (1H, s, ArH), 7.17 (1H, s, ArH), 7.14 (1H, s, ArH), 6.62 (1H, d, ArH), 2.19 (3H, d, CH_3); δ_C (75 MHz; $CDCl_3$) 187.9, 187.7, 146.0, 142.6, 136.7, 136.6, 133.5, 131.4, 130.3, 121.0, 118.0, 116.4, 15.9.

2-(4-Fluoroanilino)-5-methyl-1,4-benzoquinone (3e).[2] Toluhydroquinone (277 mg, 2.24 mmol) and 4-fluoroaniline (100 µL, 1.04 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 15 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give **3e** (134 mg, 56%) as a purple solid. mp 176 °C; λ_{max} ($CHCl_3$)/nm 495 (ε 2230), 283 (6050), 266 (3210), 261 (3130); ν_{max} (solid)/cm^{-1} 3182, 1676, 1643, 1576, 1506, 1411, 1218, 888, 819; δ_H (300 MHz; $CDCl_3$) 7.17 (2H, m, ArH), 7.08 (2H, m, ArH), 6.55 (1H, s), 6.00 (1H, s), 2.08 (3H, s); δ_C (75 MHz; $CDCl_3$) 186.9, 184.0, 150.0, 143.9, 129.6, 124.8, 124.7, 117.0, 116.7, 100.9, 16.7; HRMS (ESI) Found: MNa^+, 254.0587. $C_{13}H_{10}FNO_2Na^+$ requires 254.0588.

and **2-(4-fluoroanilino)-6-methyl-1,4-benzoquinone (7e)**[2] (34 mg, 14%) as a purple solid, mp 140 °C. λ_{max} ($CHCl_3$)/nm 495 (ε 2500), 288 (5630); ν_{max} (solid)/cm^{-1} 3263, 2921, 1672, 1646, 1581, 1502, 1410, 1341, 1274, 1214, 1188, 903, 826; δ_H (300 MHz; $CDCl_3$) 7.17 (2H, m, ArH), 7.08 (2H, m, ArH), 6.51 (1H, m), 5.95 (1H, m), 2.07 (3H, m); δ_C (75 MHz; $CDCl_3$) 187.0, 184.7, 162.1, 158.9, 144.0, 141.6, 136.3, 133.8, 125.0, 117.0, 100.8, 15.8; HRMS (ESI) Found: MNa^+, 254.0591. $C_{13}H_{10}FNO_2Na^+$ requires 254.0588.

2-(4-Bromoanilino)-5-methyl-1,4-benzoquinone (3f). Toluhydroquinone (147 mg, 1.18 mmol) and 4-bromoaniline (103 mg, 0.60 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 10 minutes. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 5% ethyl acetate-hexanes, to give **2f** (47 mg, 27%) as a dark purple solid. mp 157 °C; HRMS (ESI) Found: MH^+, 291.9964. $C_{13}H_{11}BrNO_2^+$ requires 291.9968; λ_{max} ($CHCl_3$)/nm 498 (ε 2350), 288 (11 700); ν_{max} (solid)/cm^{-1} 3237, 1674, 1643, 1575, 1512, 1488, 1299, 886, 818; δ_H (300 MHz; $CDCl_3$) 7.50 (2H, m, ArH), 7.10 (2H, m, ArH), 6.58 (1H, m), 6.13 (1H, s), 2.10 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 186.8, 183.7, 179.4, 149.8, 142.7, 136.8, 132.1, 129.5, 123.6, 122.8, 118.3, 101.6, 16.5;

and **2-(4-bromoanilino)-6-methyl-1,4-benzoquinone (7f)** (34 mg, 19%) as a dark purple solid. mp 150 °C; HRMS (ESI) Found: MH^+, 291.9965. $C_{13}H_{11}BrNO_2^+$ requires 291.9968; λ_{max} ($CHCl_3$)/nm 495 (ε 2560), 288 (9440); ν_{max} (solid)/cm^{-1} 2926, 1712, 1602, 1585, 1361, 1266, 1221, 732, 530; δ_H (300 MHz; $CDCl_3$) 7.50 (2H, m, ArH), 7.10 (2H, m, ArH), 6.54 (1H, m), 6.10 (1H, m), 2.09 (3H, m, CH_3); δ_C (75 MHz; $CDCl_3$) 186.8, 184.4, 142.8, 141.6, 136.9, 136.1, 132.9, 123.8, 118.4, 101.5, 15.6.

2-(4-Iodoanilino)-5-methyl-1,4-benzoquinone (2g) and 2-(4-iodoanilino)-6-methyl-1,4-benzoquinone (7g). Toluhydroquinone (133 mg, 1.07 mmol) and 4-iodoaniline (110mg, 0.50 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 18 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give an inseparable mixture of **2g** and **7g** (46 mg, 27%) as a dark solid; λ_{max} ($CHCl_3$)/nm 518 (ε 3200), 380 (1420), 291 (9290); ν_{max} (solid)/cm^{-1} 3294, 2923, 2854, 1644, 1558, 1482, 1393, 1268, 1215, 1125, 1057, 1004, 880, 814; δ_H (300 MHz; $CDCl_3$) 7.65 (2H, m, ArH), 7.37 (1H, s, ArH), 6.81 (2H, m, ArH), 6.58 (1H, s, ArH), 2.18 (3H, s, CH_3), 2.10 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 181.4, 181.0, 148.5, 147.0, 141.9, 138.8, 137.8, 136.8, 134.4, 129.6, 127.1, 126.9, 123.8, 89.9, 89.8, 17.9, 15.5; HRMS (ESI) Found MH^+ 339.9822. $C_{13}H_{11}INO_2^+$ requires 339.9829.

2-(4-Ethoxyanilino)-5-methyl-1,4-benzoquinone (2h). Toluhydroquinone (197 mg, 1.59 mmol) and 4-ethoxyaniline (100 µL, 0.77 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 10 minutes. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give **2h** (140 mg, 70%) as a purple solid, mp 122 °C; λ_{max} ($CHCl_3$)/nm 518 (ε 5430), 283 (1680), 263 (1340), 258 (1270); ν_{max} (solid)/cm^{-1} 3262, 2977, 2924, 1639, 1579, 1499, 1282, 1217, 1169, 821; δ_H (300 MHz; $CDCl_3$) 7.12 (2H, m, ArH), 6.90 (2H, m, ArH), 6.53 (1H, m), 5.97 (1H, s), 4.03 (2H, q, $CH_3C\underline{H}_2O$), 2.08 (1H, s, CH_3), 1.42 (3H, t, $C\underline{H}_3CH_2O$); δ_C (75 MHz; $CDCl_3$) 186.8, 184.3, 157.2, 150.2, 144.3, 130.3, 129.5, 124.6, 115.8, 100.2, 64.1, 16.8, 15.1; *m/z* (APCI) 512 (47%), 258 (M^+, 100), 213 (24); HRMS (APCI) Found: MNa^+, 280.0944. $C_{15}H_{15}NO_3Na^+$ requires 280.0950

and **2-(4-ethoxyanilino)-6-methyl-1,4-benzoquinone (7h)** (49 mg, 25%) as a purple solid. mp 159 °C, λ_{max} ($CHCl_3$)/nm 518 (ε 450), 284 (1510); ν_{max} (solid)/cm^{-1} 3244, 2979, 2924, 1644, 1574, 1514, 1473, 1244; δ_H (300 MHz; $CDCl_3$) 7.12 (2H, m, ArH), 6.90 (2H, m, ArH), 6.50 (1H, m), 5.94 (1H, s), 4.03 (2H, q, $CH_3C\underline{H}_2O$), 2.07 (1H, s, CH_3), 1.42 (3H, t, $C\underline{H}_3CH_2O$); δ_C (75 MHz; $CDCl_3$) 186.8, 184.7, 157.1, 144.2, 141.2, 136.4, 130.2, 124.6, 115.6, 100.0, 64.0, 15.5, 14.9.HRMS (APCI) Found: MNa^+, 280.0944. $C_{15}H_{15}NO_3Na^+$ requires 280.0950.

2-(4-Acetamidoanilino)-5-methyl-1,4-benzoquinone (2i) and **2-(4-acetamidoanilino)-6-methyl-1,4-benzoquinone (7i)**. Toluhydroquinone (169 mg, 1.36 mmol) and 4-aminoacetaniline (99 mg, 0.66 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 6 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (5 × 50 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 50% ethyl acetate-hexanes, to give an inseparable mixture of **2i** and **7i** (71 mg, 40%) as a purple solid; (Found: MNa^+, 293.0897. $C_{15}H_{14}N_2O_3Na^+$ requires 293.0902); λ_{max} ($CHCl_3$)/nm 513 (ε 1520), 285 (7140), 263 (3910); ν_{max} (solid)/cm^{-1} 3295, 3191 (NH), 3077, 1674 (CO), 1575, 1524, 1409; δ_H (300 MHz; DMSO-d^6) 10.03 (1H, s, NH), 8.88 (1H, s, NH), 7.63 (2H, m, ArH), 7.29 (2H, m, ArH), 6.69 (1H, s), 6.56 (1H, s), 5.85 (1H, s), 5.79 (1H, d), 2.08 (3H, s, CH_3), 2.02 (3H, s, CH_3); δ_C (75 MHz; DMSO-d^6) 186.5, 186.4, 184.8, 184.7, 169.2, 149.4, 145.5, 145.4, 142.3, 137.4, 136.0, 134.0, 133.9, 130.4, 124.7, 124.6, 120.6, 100.0, 99.9, 24.8, 16.8, 14.9; *m/z* (APCI) 271 (M^+, 100%), 229 (20), 213 (6).

2-(4-Nitroanilino)-5-methyl-1,4-benzoquinone (2j). Toluhydroquinone (173 mg, 1.39 mmol) and 4-nitroaniline (99 mg, 0.72 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 48 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 50% dichloromethane-toluene, to give **2j** (37 mg, 20%) as a red solid. mp 218 °C; HRMS (ESI) Found: MH^+, 259.0710. $C_{13}H_{11}N_2O_4^+$ requires 259.0713; λ_{max} ($CHCl_3$)/nm 467 (ε 1370), 331 (3860); ν_{max} (solid)/cm^{-1} 2921, 2852, 1567, 1502, 1328, 1111, 1024, 1003; δ_H (200 MHz; DMSO-d^6) 9.35 (1H, br s, NH), 8.23 (2H, d, ArH), 7.60 (2H, d, ArH), 6.78 (1H, d, ArH), 6.30 (1H, s, ArH), 2.00 (3H, d, CH_3); δ_C (50 MHz; DMSO-d^6) 186.5, 183.3, 147.7, 145.3, 142.5, 142.3, 130.2, 125.1, 121.3, 104.1, 15.6;

and **2-(4-nitroanilino)-6-methyl-1,4-benzoquinone (7j)** (42 mg, 23%) as a red solid. mp 215 °C; HRMS (ESI) Found: MH^+, 259.0707. $C_{13}H_{11}N_2O_4^+$ requires 259.0713; λ_{max} ($CHCl_3$)/nm 472 (ε 2070), 331 (5910); ν_{max} (solid)/cm^{-1} 2926, 1711, 1420, 1360, 1268, 1221, 732, 529; δ_H (300 MHz; DMSO-d^6) 9.35 (1H, br s, NH), 8.22 (2H, d, ArH), 7.59 (2H, d, ArH), 6.62 (1H, s, ArH), 6.23 (1H, d, ArH), 2.01 (3H, d, CH_3); δ_C (50 MHz; DMSO-d^6) 186.6, 183.6, 145.5, 142.6, 142.4, 142.2, 134.2, 125.1, 121.3, 104.0, 15.2.

2-(4-Fluoroanilino)-1,4-naphthoquinone (9).[6, 7] Naphthohydroquinone (103 mg, 0.642 mmol) and 4-fluoroaniline (30 µL, 0.31 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 10 minutes. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give **9** (33 mg, 39%) as a red solid, mp 242 °C (lit., mp 244 °C); (Found: MNa^+, 267.0690. $C_{16}H_{10}NO_2FNa^+$ requires 267.0696); λ_{max} (MeOH)/nm 461 (ε 4020), 291 (11 100); ν_{max} (solid)/cm^{-1} 3340, 2919, 1664, 1590, 1571, 1504, 1298, 1210, 819; δ_H (300 MHz; DMSO-d^6) 9.22 (1H, s, NH), 8.07-7.74 (4H, m, ArH), 7.41 (2H, m, ArH), 7.27 (2H, m, ArH), 5.99 (1H, s); δ_C (75 MHz; DMSO-d^6) 184.8, 182.5, 181.5, 146.5, 138.7, 134.9, 134.2, 132.6, 131.5, 130.4, 126.0, 125.8, 125.3, 116.2, 115.9, 101.8; *m/z* (APCI) 269 (MH^+, 15%), 268 (100).

2-(4-Fluoroanilino)-5-bromo-1,4-benzoquinone (11). Bromohydroquinone (205 mg, 1.08 mmol) and 4-fluoroaniline (50 µL, 0.52 mmol) were taken up in aq. H_2O_2 (30% v/v; 5 mL). A catalytic amount of I_2 was added and the reaction mixture was stirred vigorously for 15 hours. The reaction mixture was poured over saturated $NaHCO_3$ solution (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic phases were dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography on silica, eluting with 10% ethyl acetate-hexanes, to give to give **11** (18 mg, 12%) as a dark solid; Found: MNa^+ 294.9638. $C_{12}H_7BrFNO_2Na^+$ requires 294.9645; λ_{max} ($CHCl_3$)/nm 516 (ε 760), 288 (4010); ν_{max} (solid)/cm^{-1}

6-Methyl-1,4,4*a*,8*a*-tetrahydro-1,4-methanonaphthalene-5,8-dione (15).[8] Toluhydroquinone (203 mg, 1.64 mmol) and cyclopentadiene (100 µL, 1.19 mmol) were taken up in aq. H_2O_2 solution (30% v/v; 5 mL). A catalytic amount of iodine was added and the reaction mixture was stirred vigorously for 45 min. Brine (50 mL) was added and the product was extracted with dichloromethane (3 × 30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purified by flash chromatography on silica, eluting with 10% ethyl acetate in hexanes to give **15** (82 mg, 50%) as a pale yellow solid; mp. 60.6-61.4 °C (lit. 62-63 °C); δ_H (300 MHz; $CDCl_3$) 6.33 (1H, s), 5.88 (2H, dd, *J* = 4.2 Hz, 2.6 Hz), 3.37 (2H, s, CH), 3.09 (2H, s, CH), 1.78 (3H, s, CH_3), 1.34 (2H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 199.4 (C), 198.9 (C), 151.5 (C), 139.5 (CH), 135.4 (CH), 134.8 (CH), 48.9 (CH), 48.8 (CH), 48.7 (CH_2), 48.5 (CH), 48.1 (CH), 16.2 (CH_3);

Triple domino cascade:

1a-methyl-2a,3,6,6a-tetrahydro-3,6-methanonaphtho[2,3-*b*]oxirine-2,7(1a*H*,7a*H*)-dione (17).[9] Toluhydroquinone (123 mg, 0.99 mmol), cyclopentadiene (68 µL, 0.81 mmol) and aniline (74 µL, 0.81 mmol) were taken up in aq. H_2O_2 solution (30% v/v; 5 mL). A catalytic amount of iodine was added and the reaction mixture was stirred vigorously for 90 min at room temperature. Poured over sat. $NaHCO_3$ solution (30 mL), extracted with dichloromethane (3 × 20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purified by flash chromatography on silica, eluting with 5% ethyl acetate/hexanes and recrystallised from ethanol to give **15** (82 mg, 50%) as a pale yellow solid; and **2** (22 mg, 13%) as a purple solid; and **17** (20 mg, 12%) as a colourless crystalline solid; mp. 138.3-138.5 °C (lit. 136-138 °C); δ_H (300 MHz; $CDCl_3$) 5.97 (2H, m, CH), 3.39 (2H, t, *J* = 2.8 Hz, CH), 3.31 (1H, s, CH), 3.22 (2H, m, CH), 1.43 (1H, m, CH_2), 1.40 (3H, s, CH_3), 1.24 (1H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 205.3, 204.8, 136.7, 136.6, 64.6, 64.2, 50.5, 49.6, 46.7, 43.4, 43.3, 14.6;

Epoxidation reactions:

Diels-Alder adduct **15** (22 mg, 0.12 mmol) and potassium carbonate (11 mg, 0.08 mmol, 70 mol%) were taken up in aq. H_2O_2 solution (5 mL, 30% v/v) and stirred vigorously at room temperature for 15 minutes. Diluted with brine solution (30 mL) and extracted with ethyl acetate (3 × 25 mL). Dried over Na_2SO_4 and solvent removed *in vacuo*. Purified by flash chromatography, eluting with 5% ethyl acetate/hexanes, to give **17** (23 mg, 97%) as an off-white solid.

Diels-Alder adduct **15** (21 mg, 0.11 mmol) and triethylamine (6 µL, 0.043 mmol, 25 mol%) were taken up in aq. H_2O_2 solution (5 mL, 30% v/v) and stirred vigorously at room temperature for 15 minutes. Diluted with brine solution (30 mL) and extracted with ethyl acetate (3 × 25 mL). Dried over Na_2SO_4 and solvent removed *in vacuo*. Purified by flash chromatography, eluting with 5% ethyl acetate/hexanes, to give **17** (23 mg, 100%) as an off-white solid.

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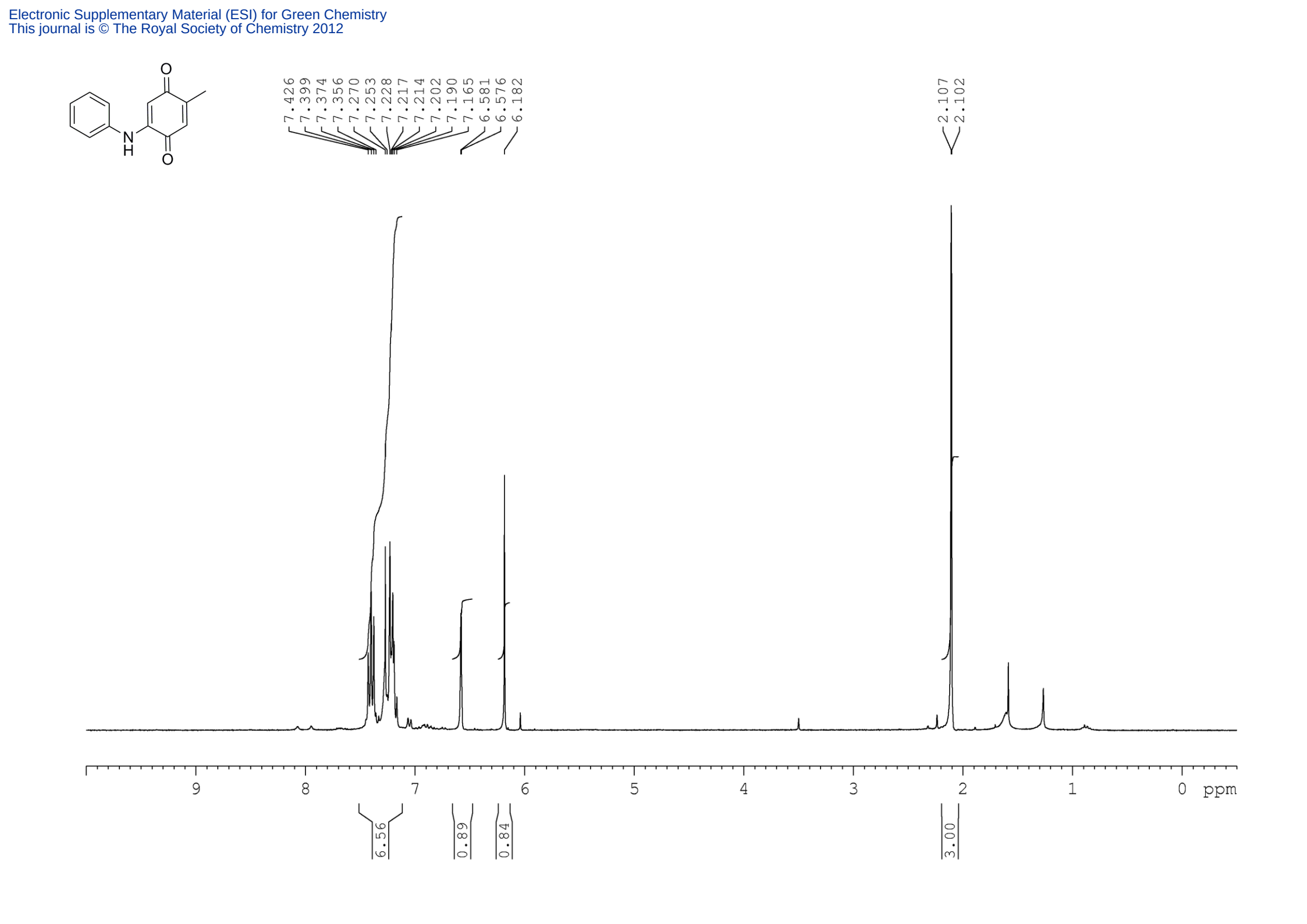

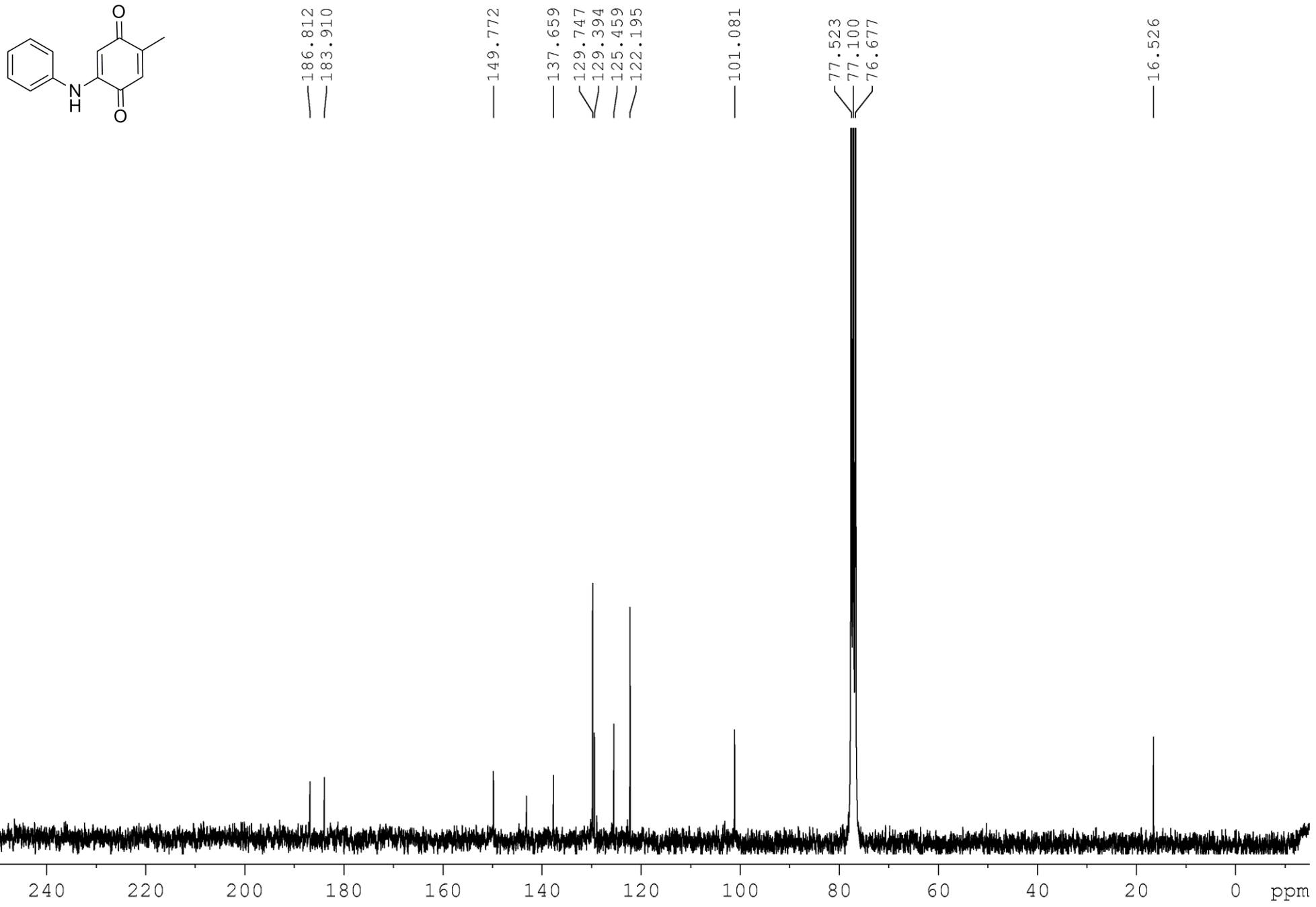

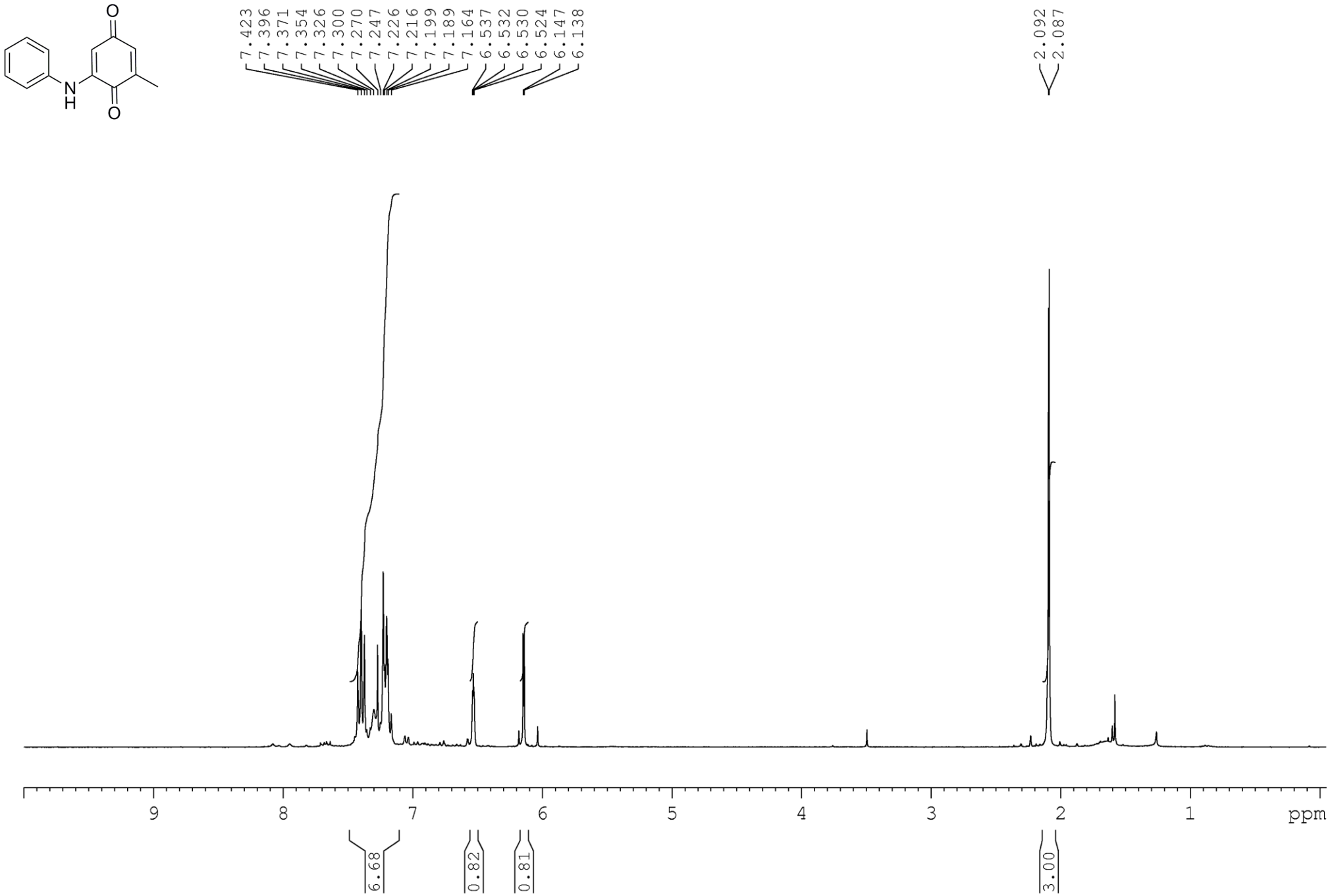

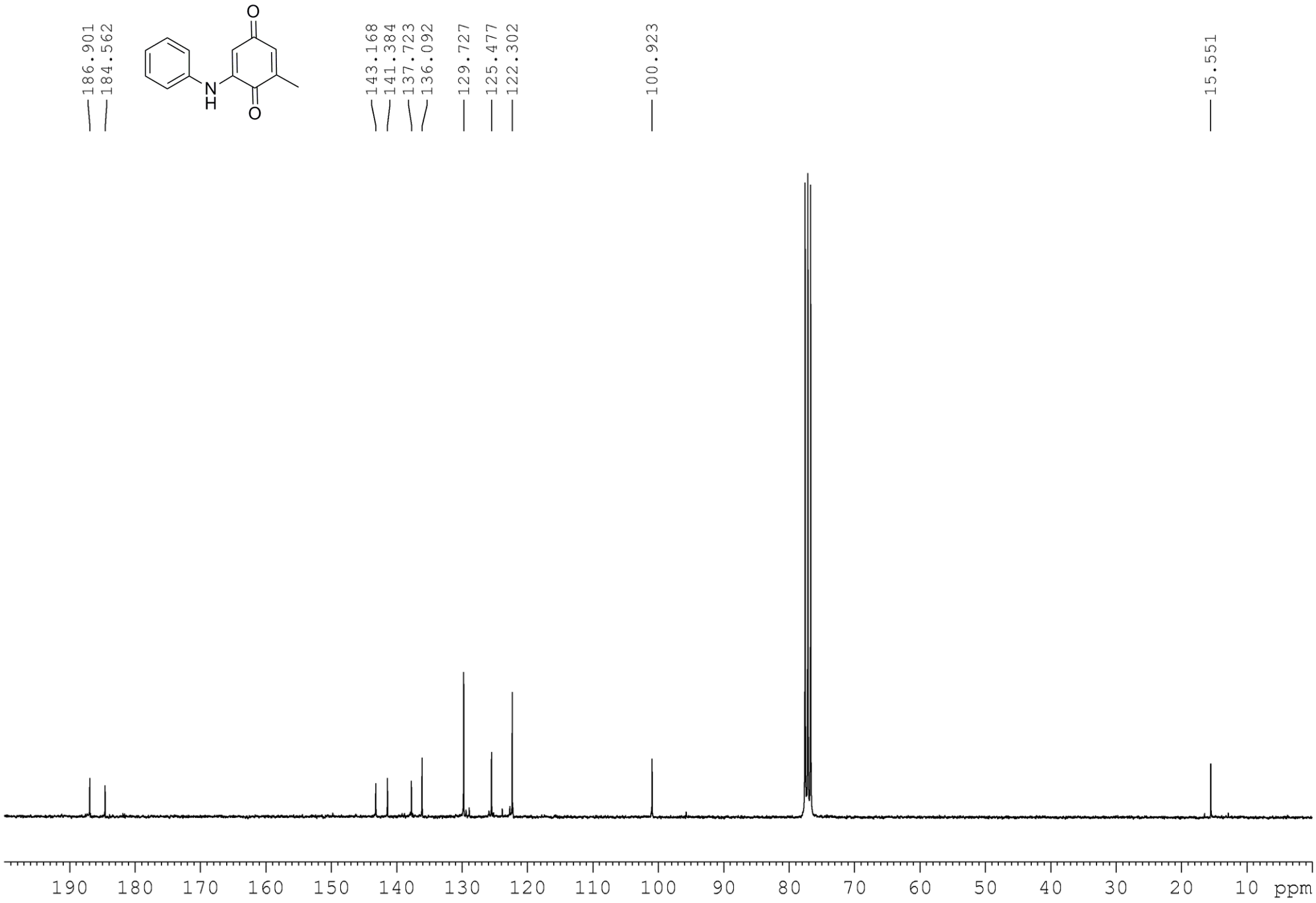

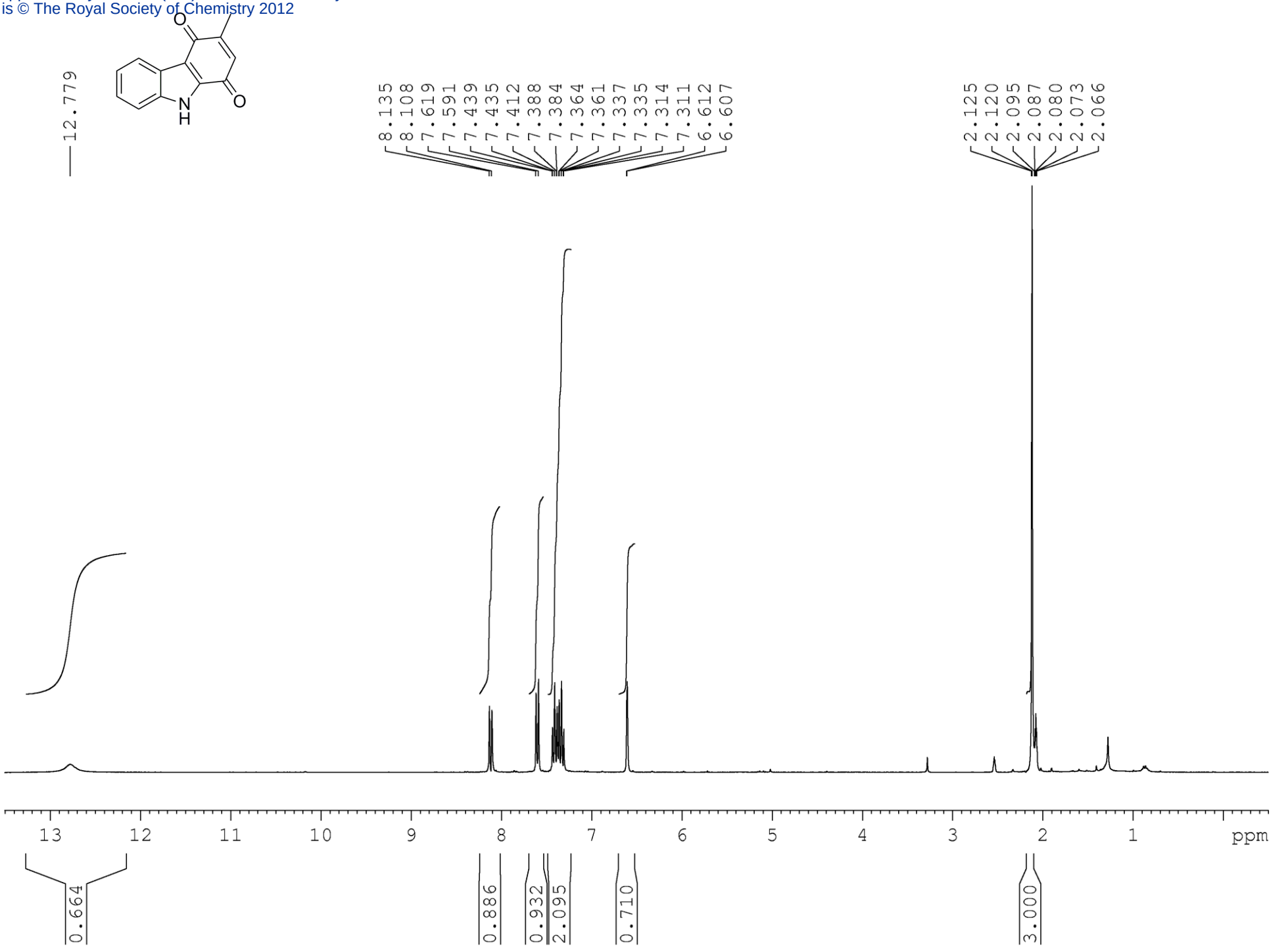

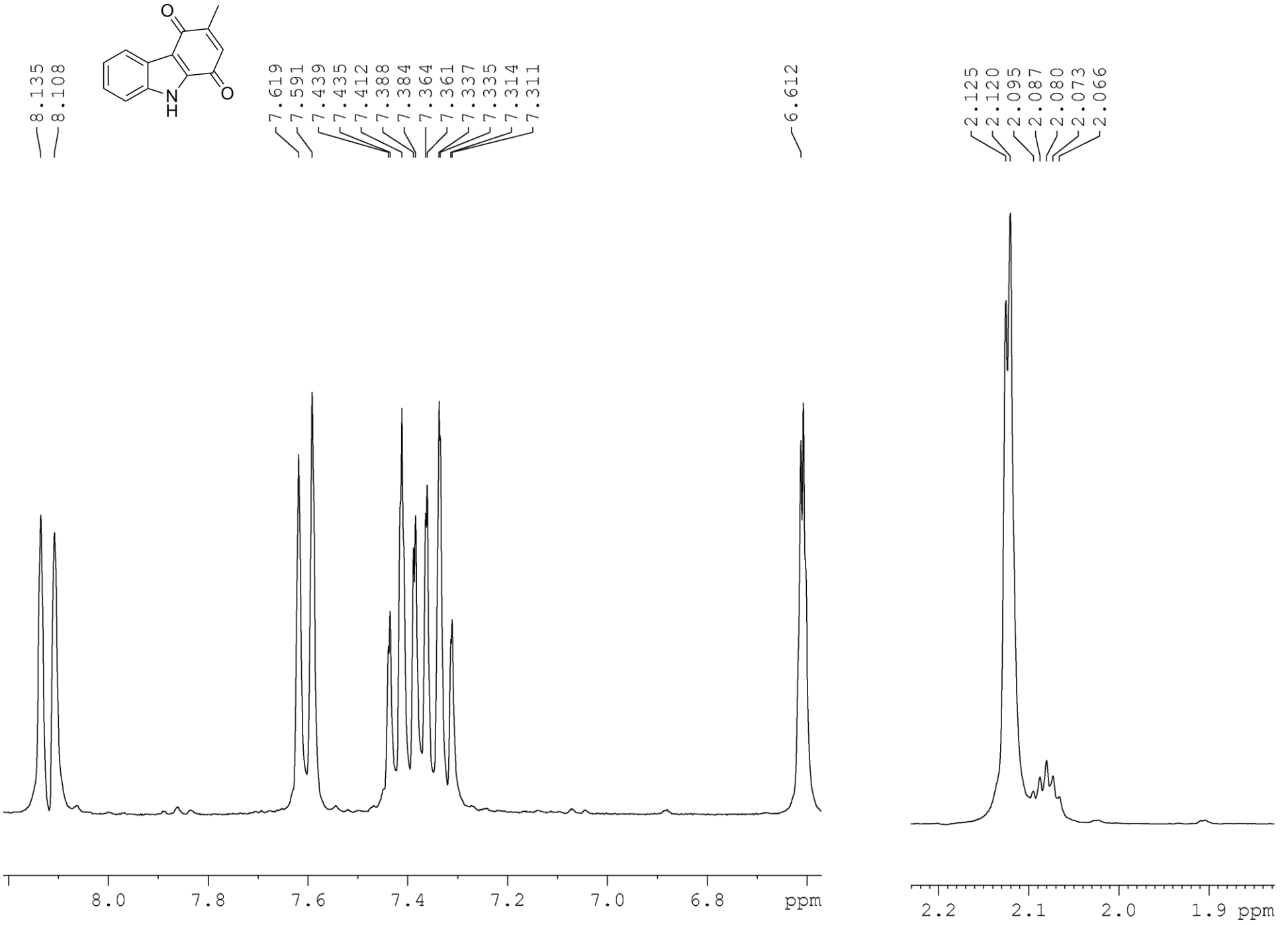

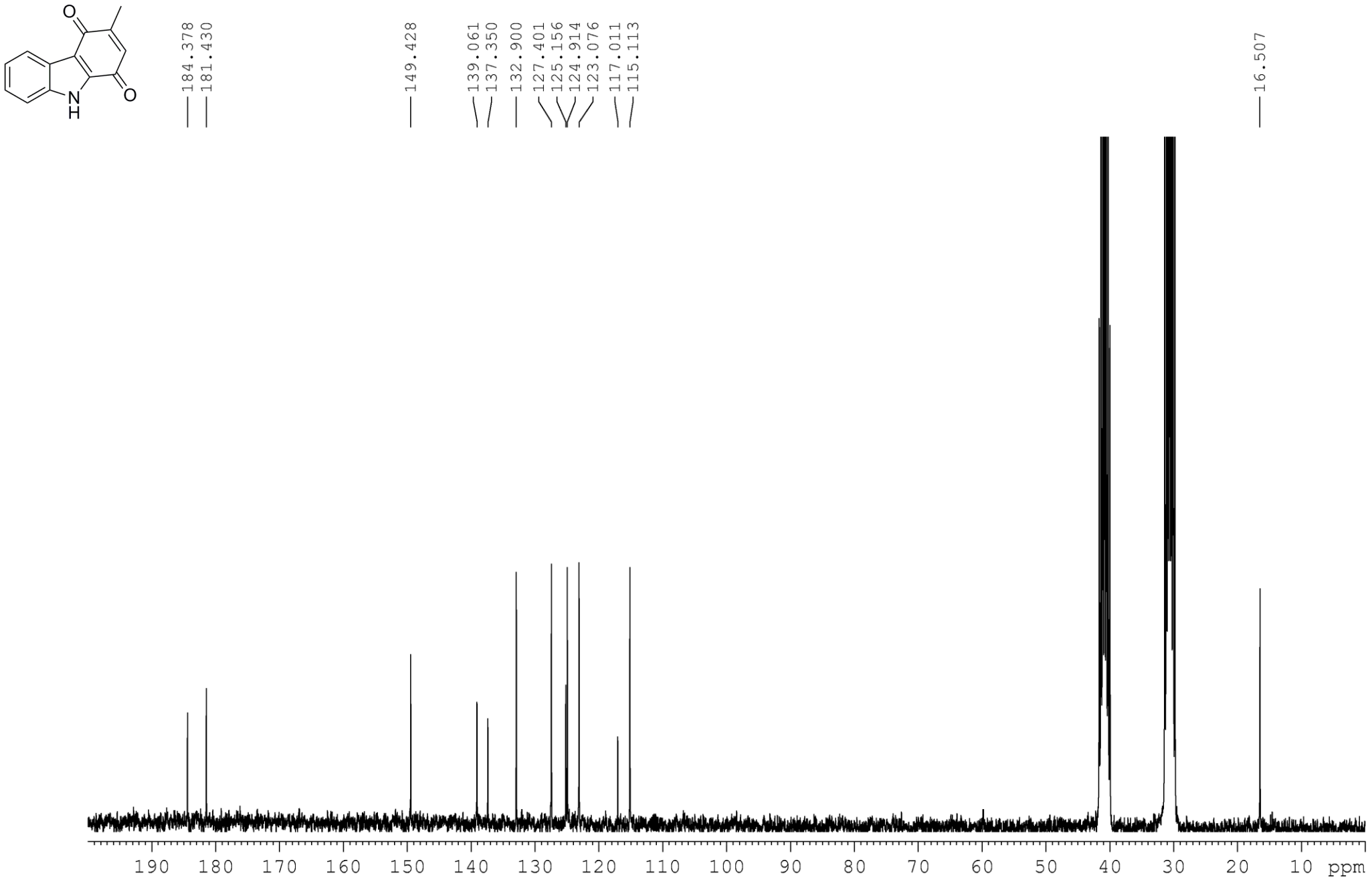

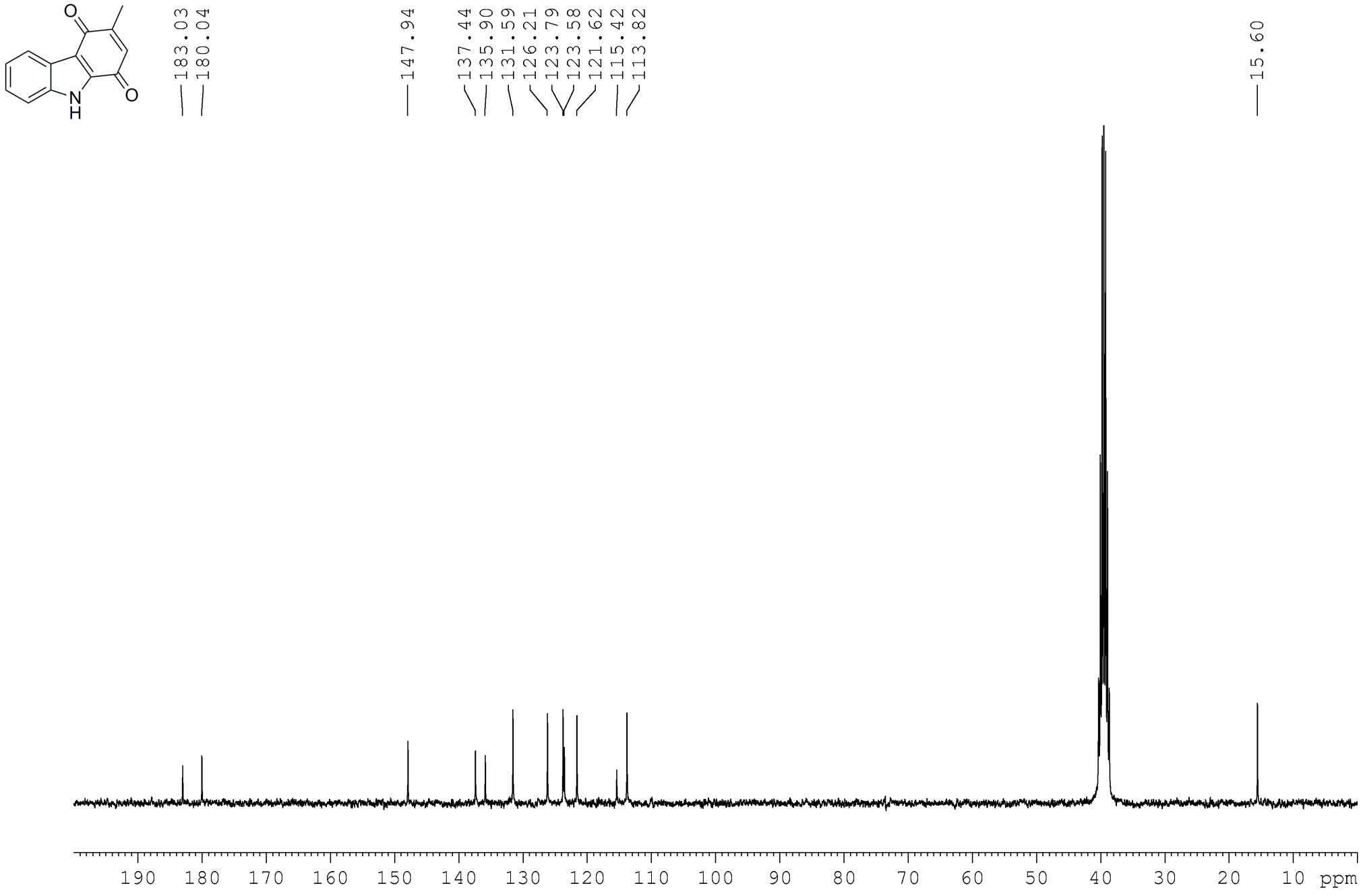

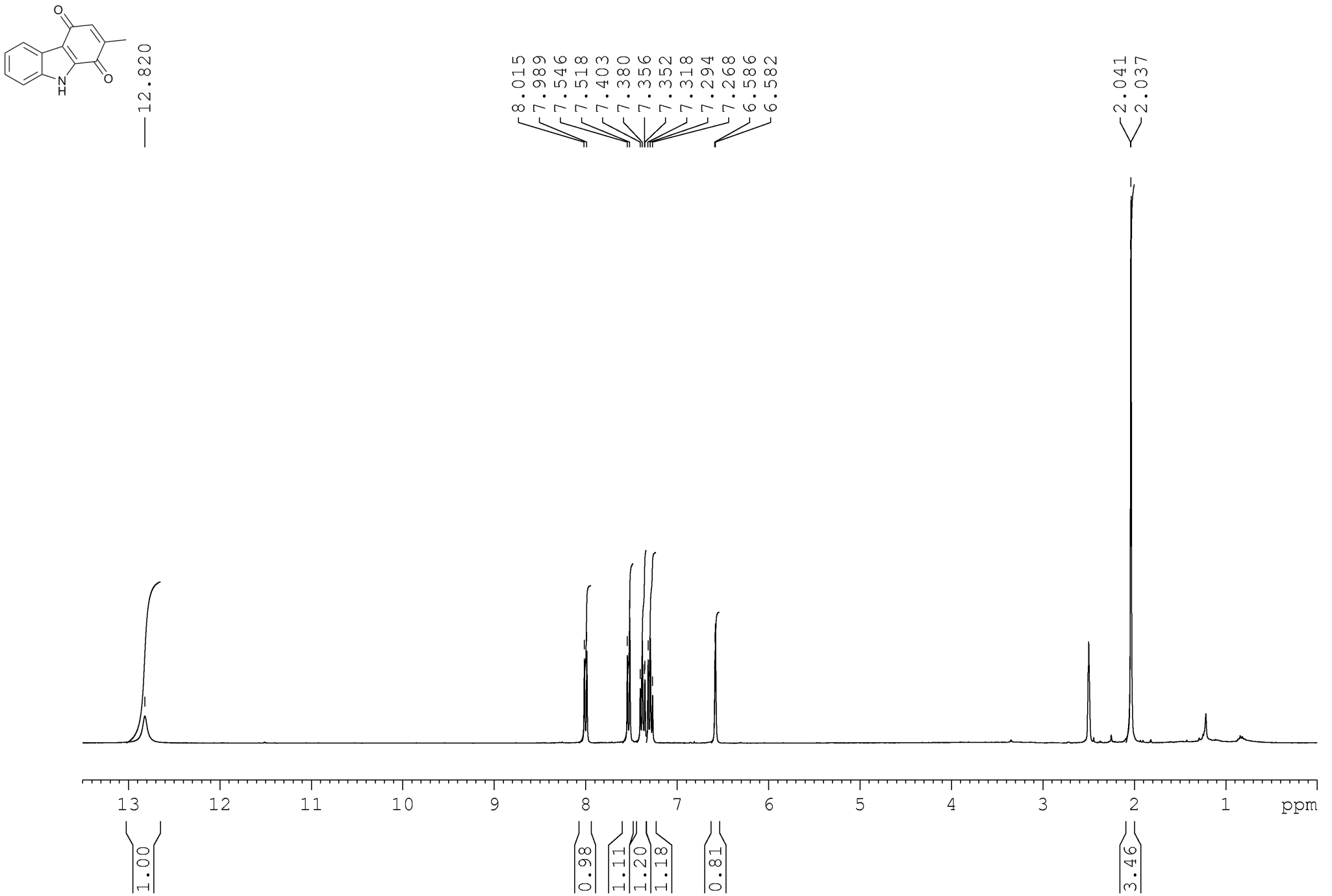

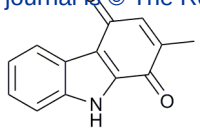

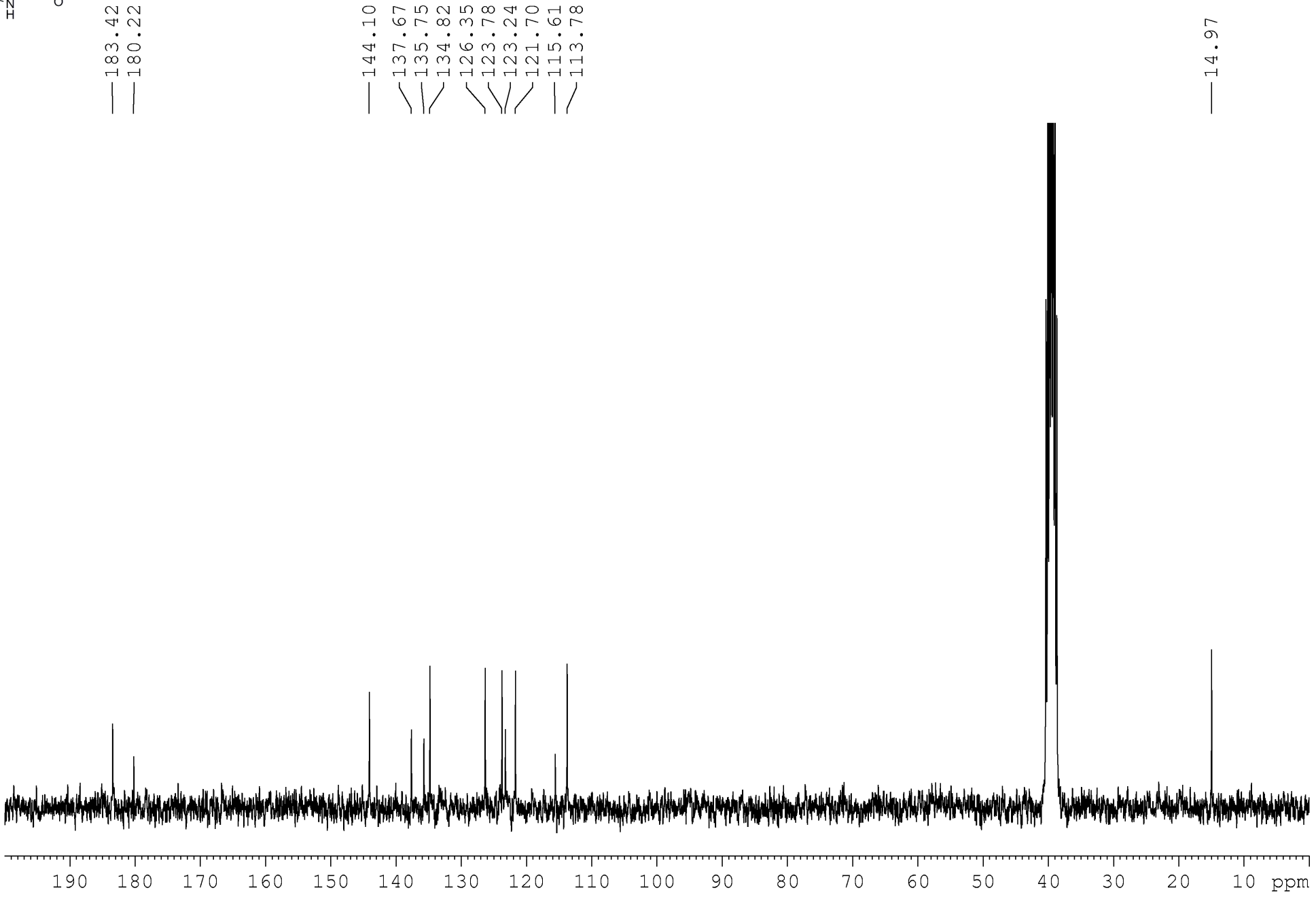

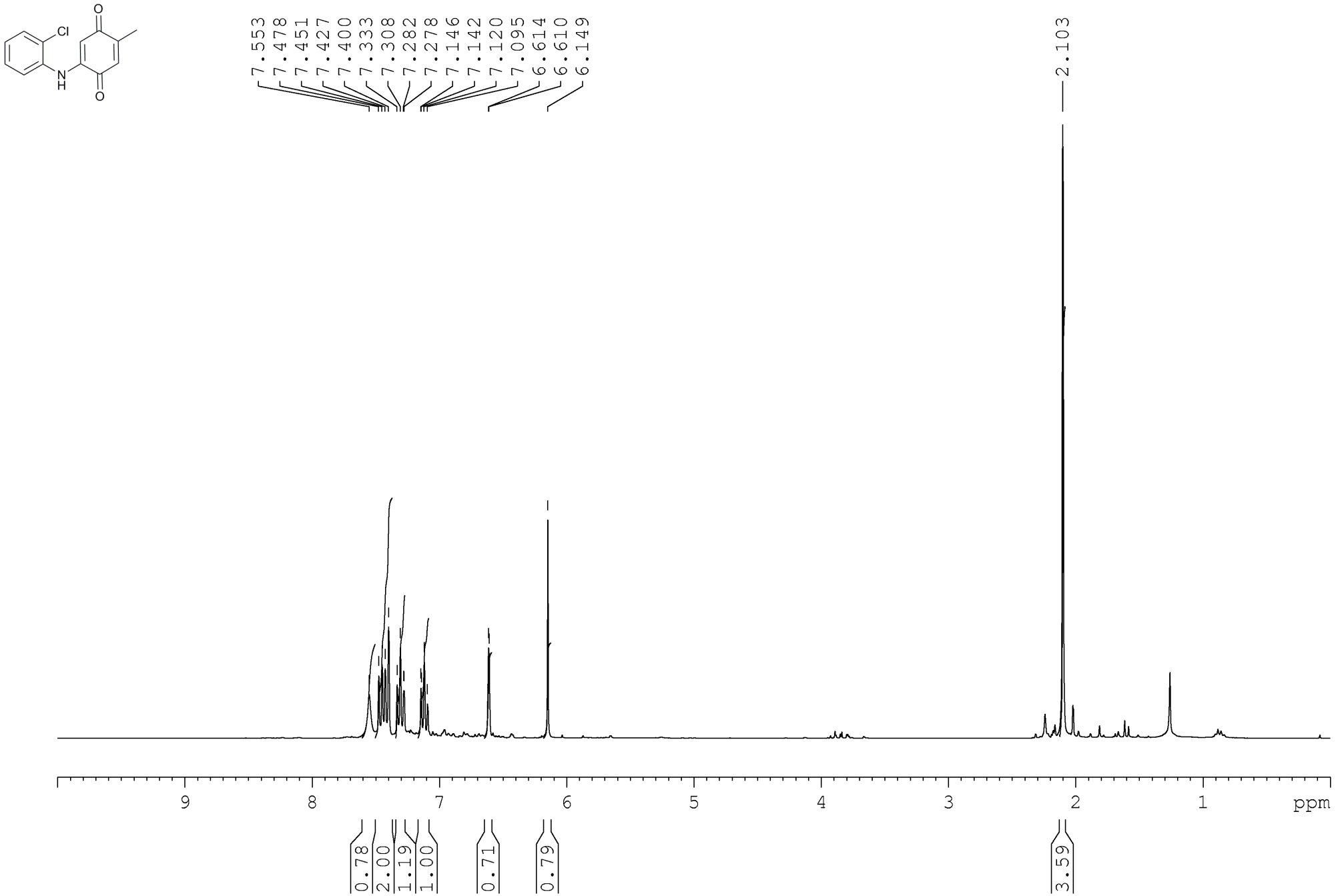

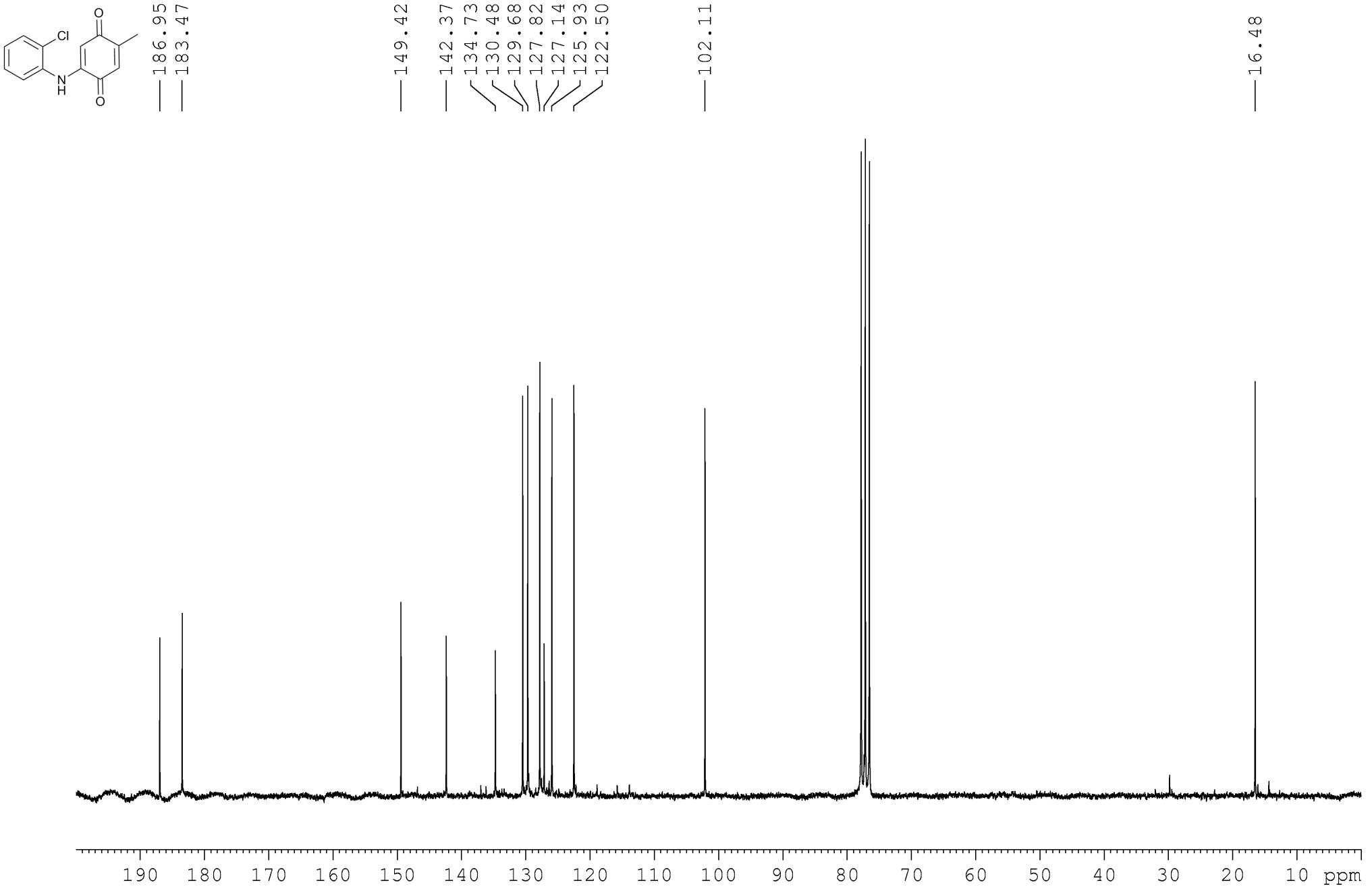

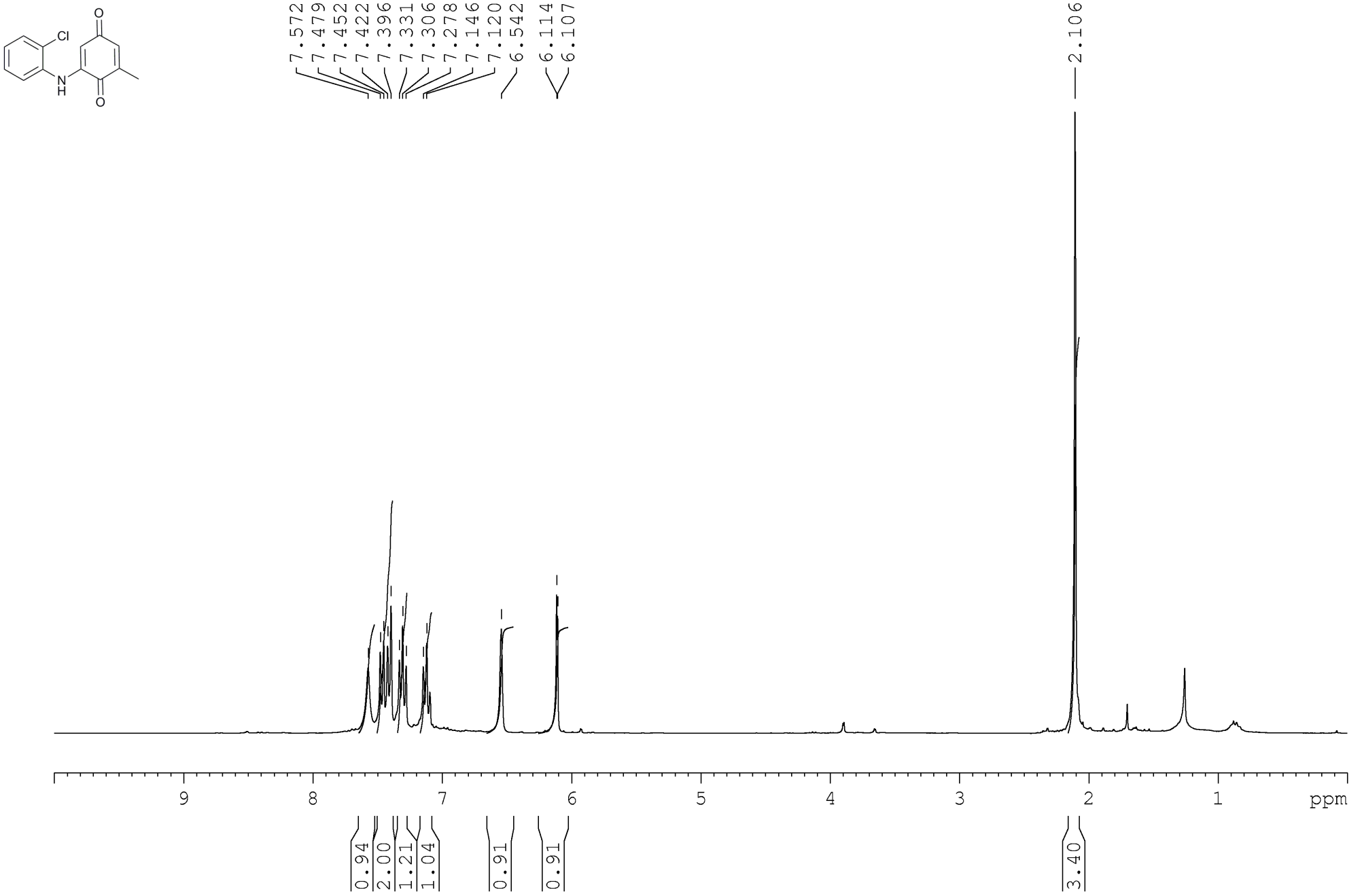

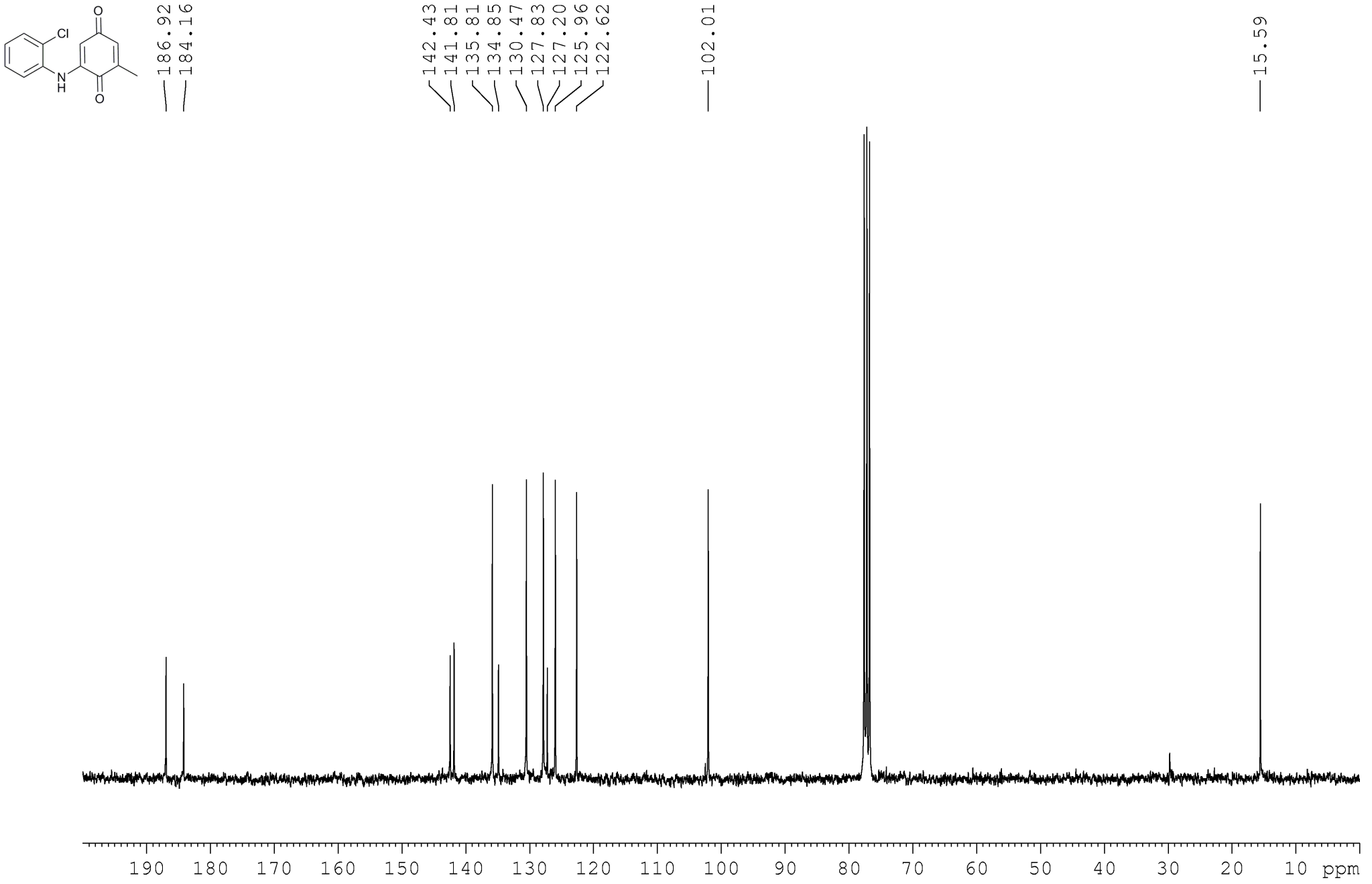

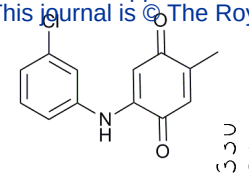

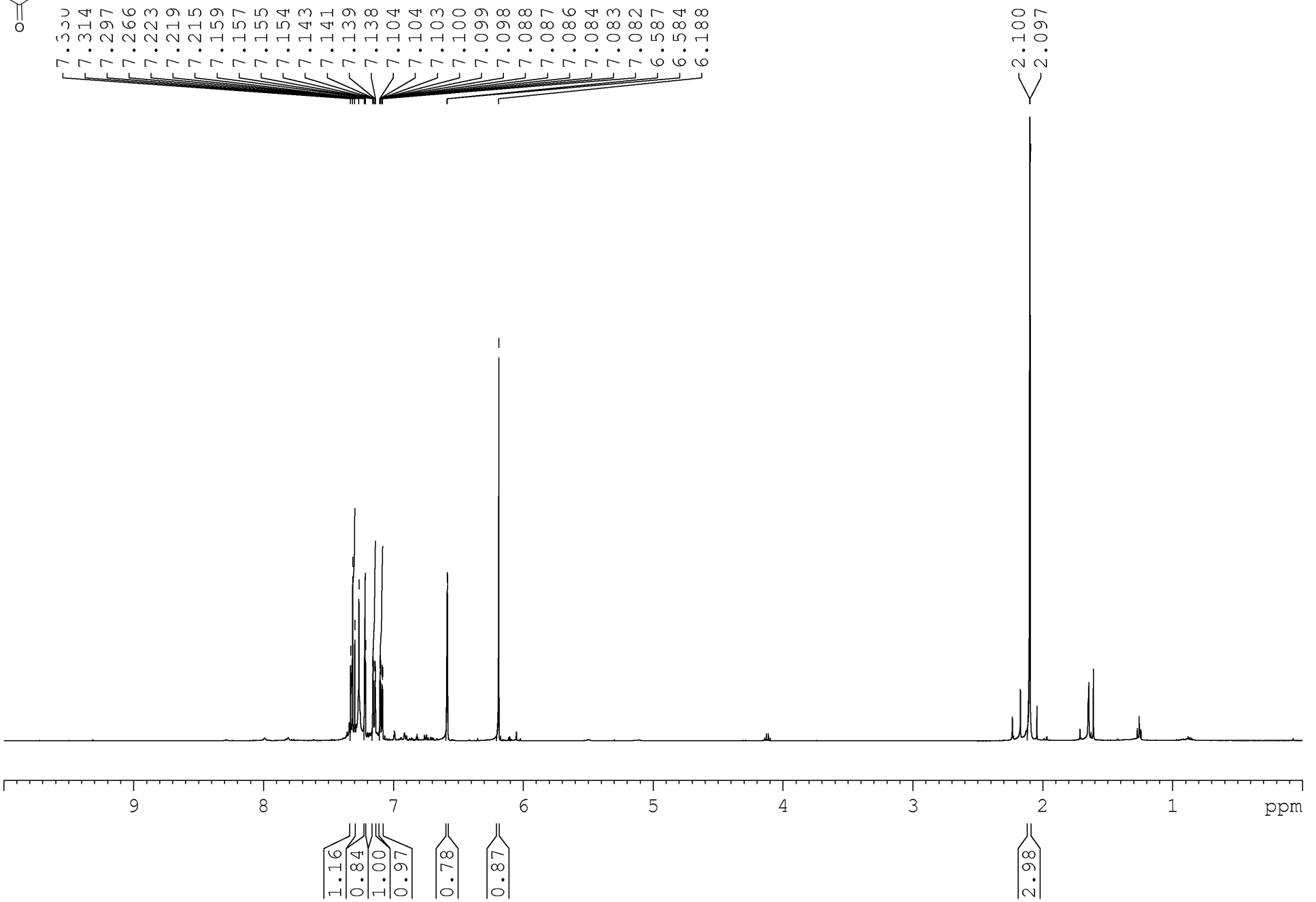

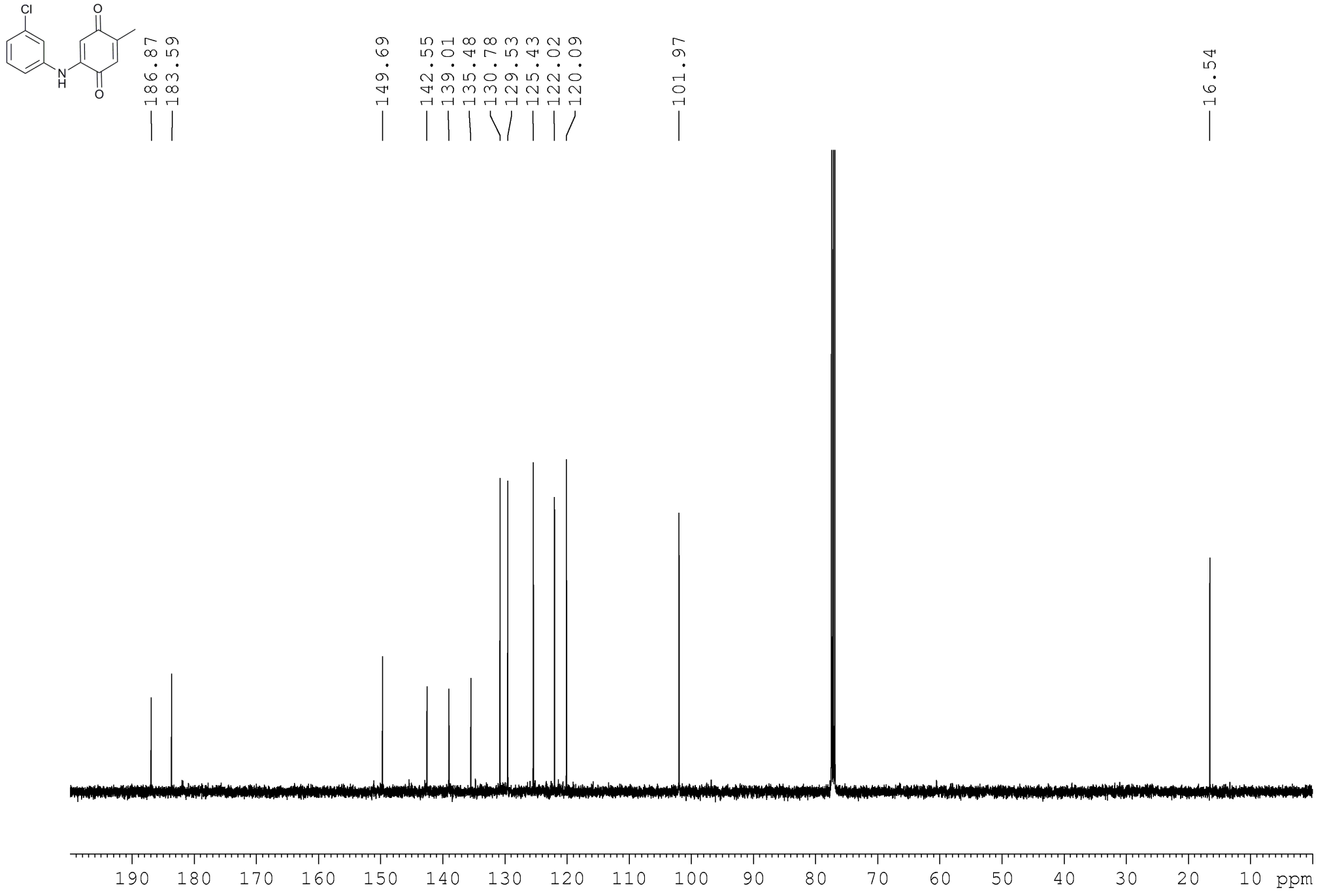

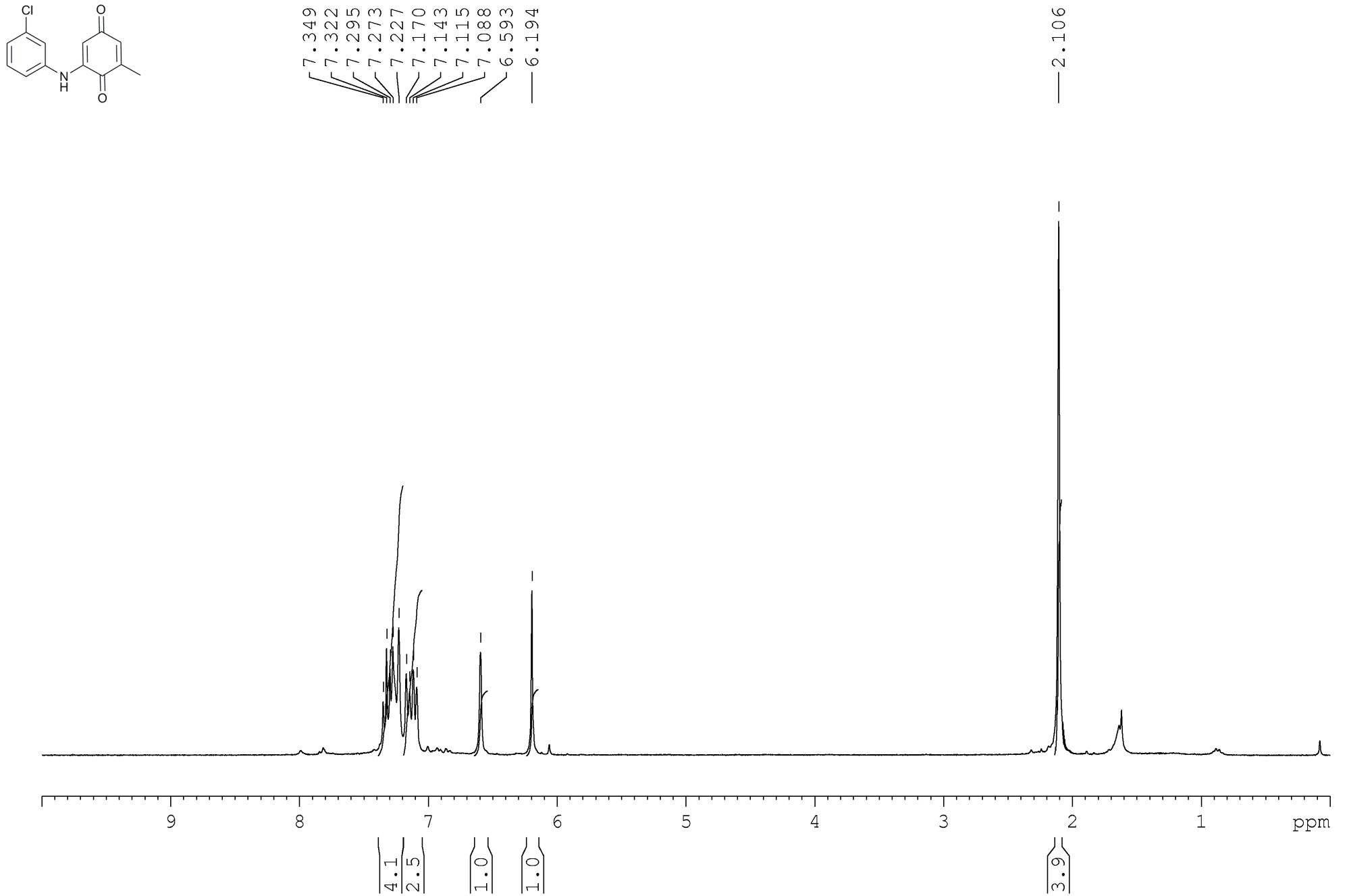

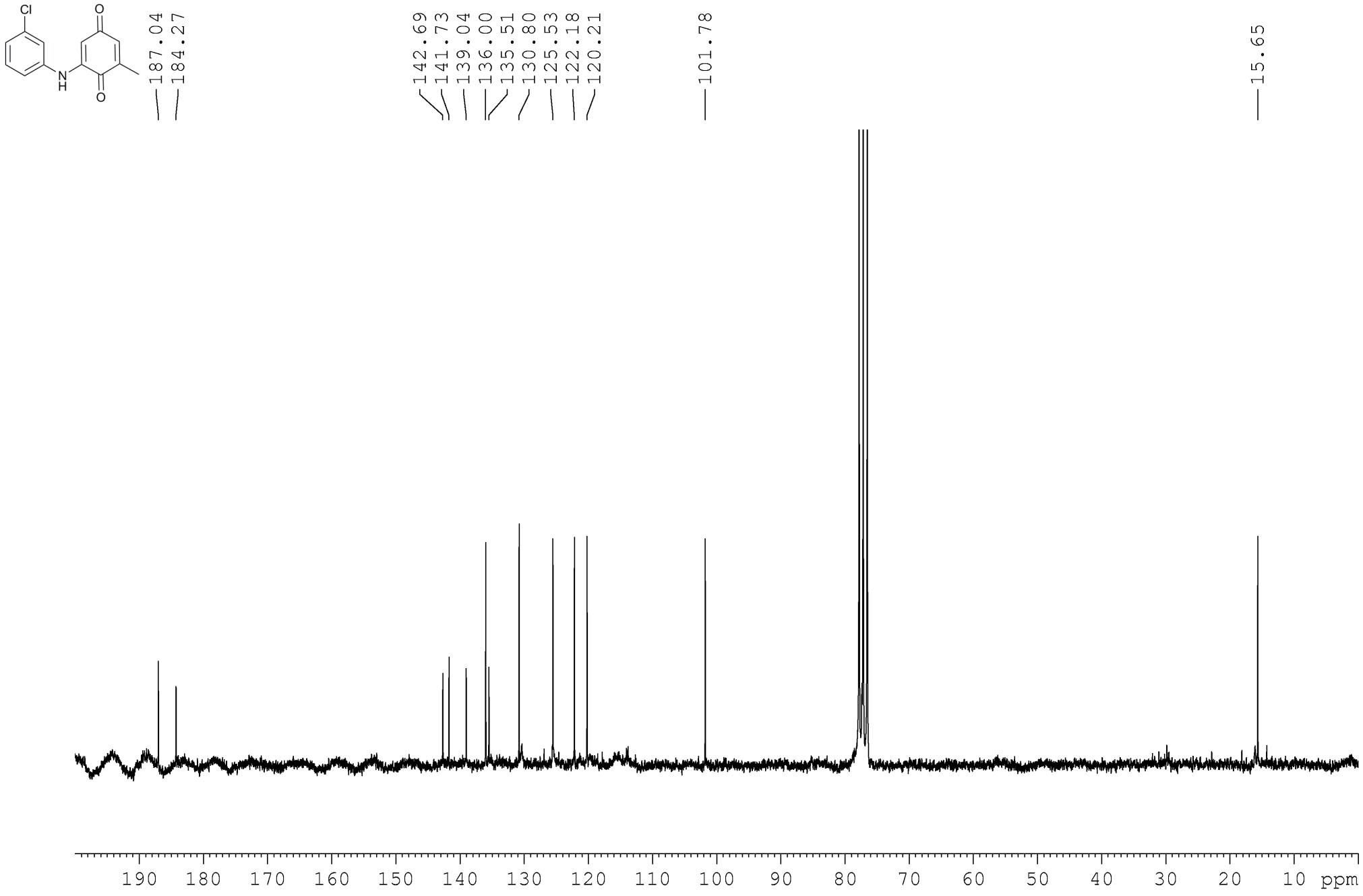

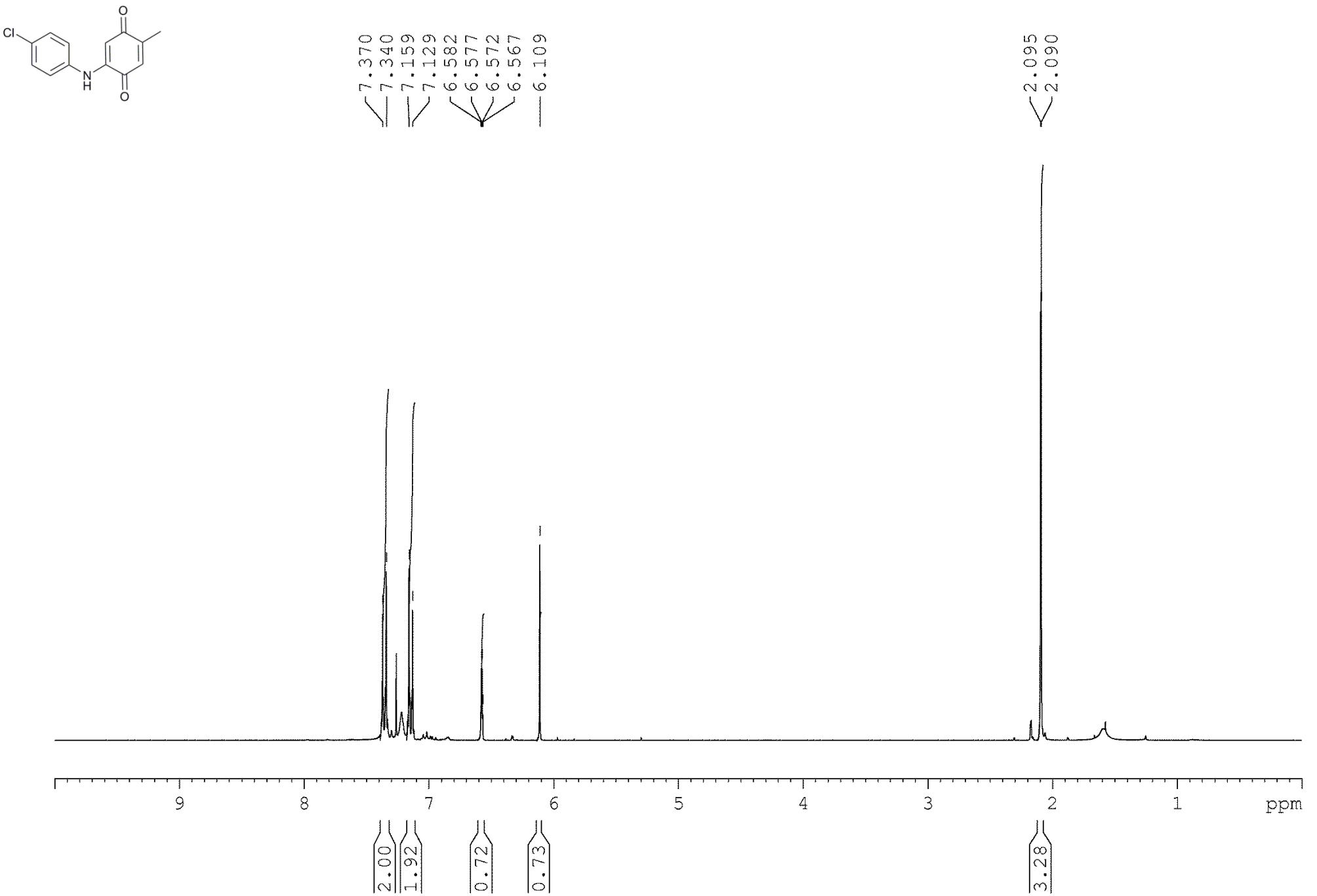

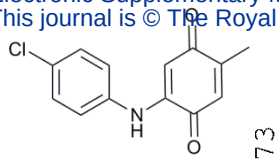

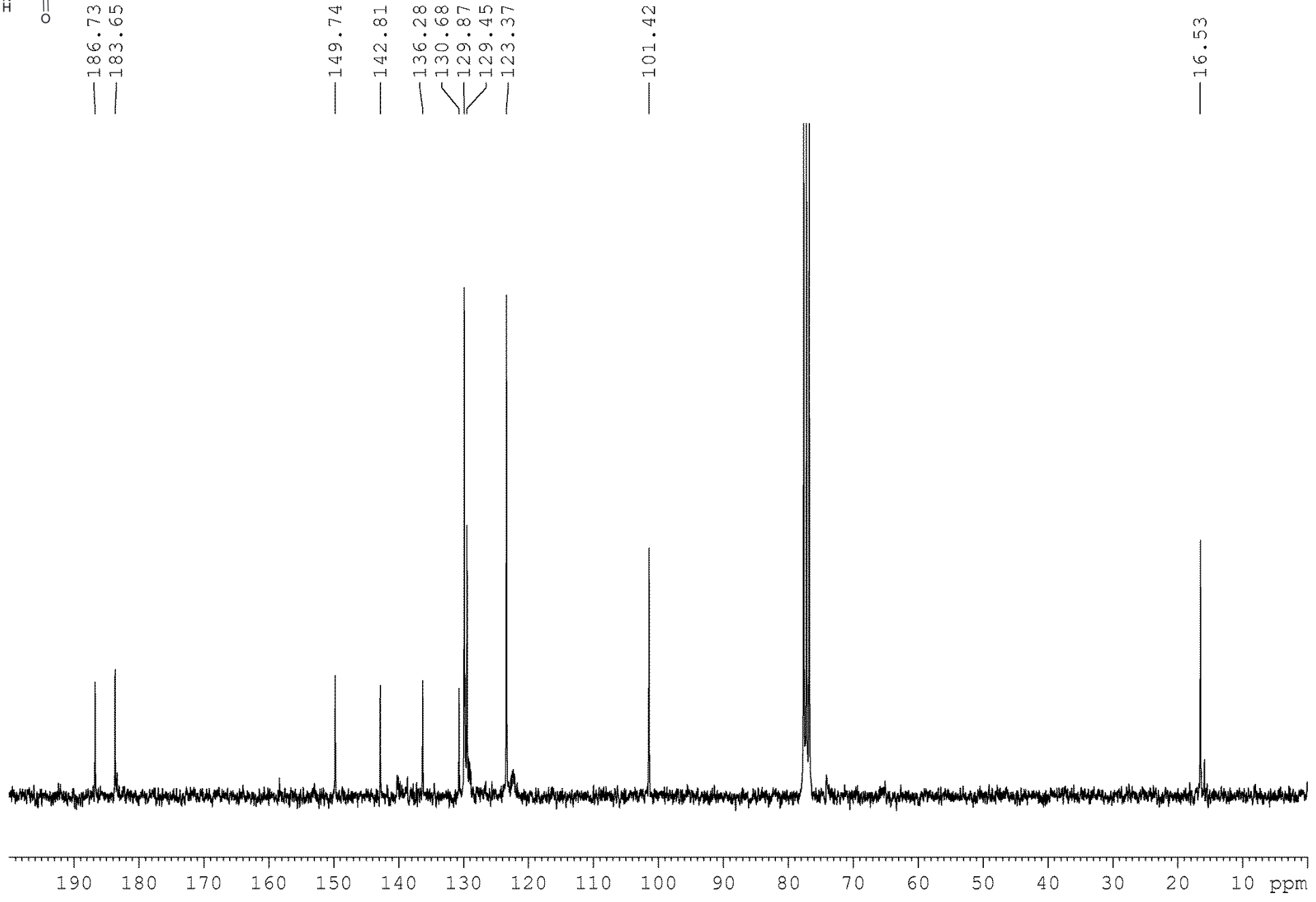

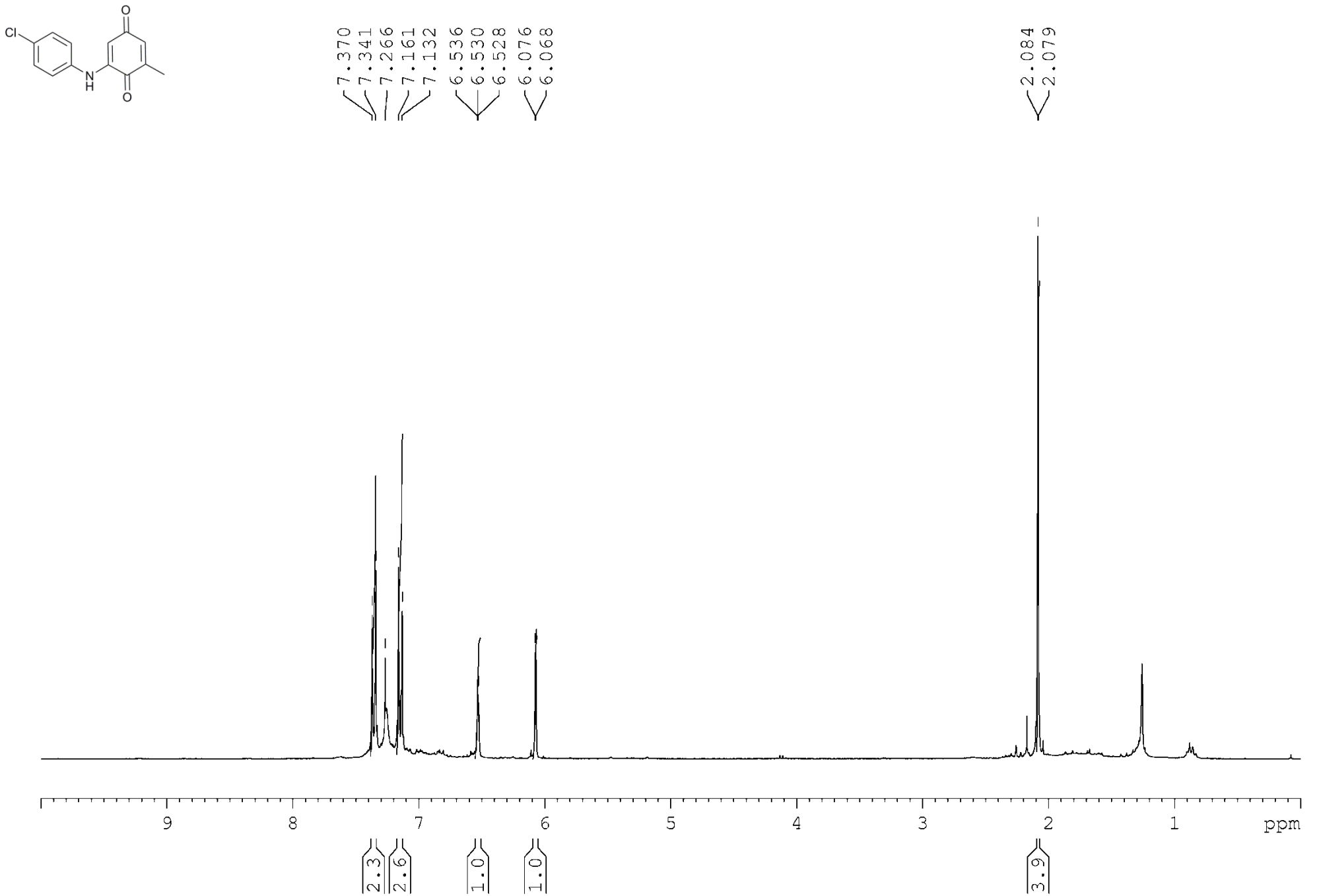

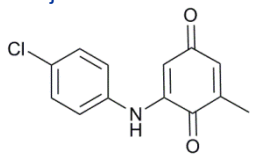

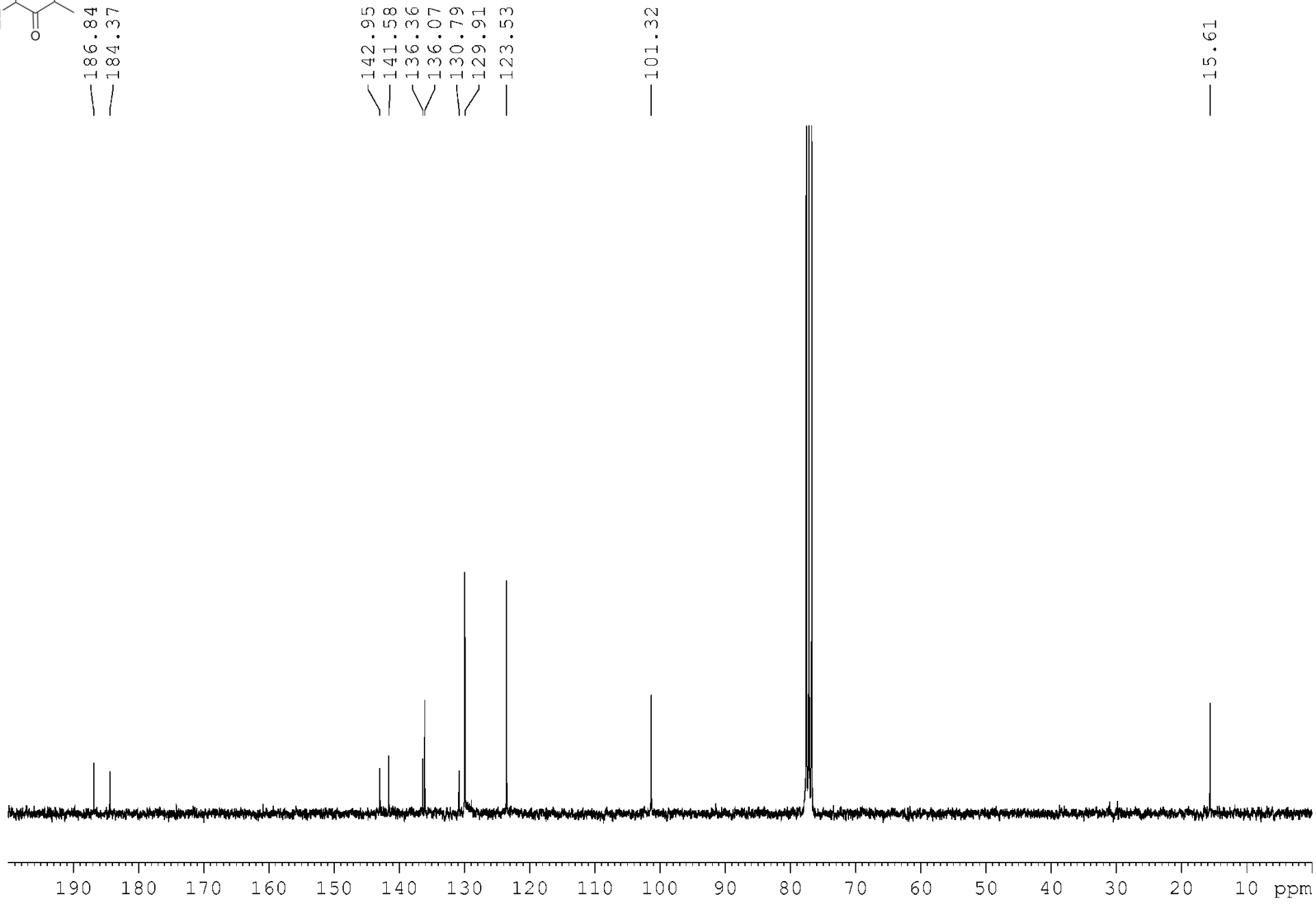

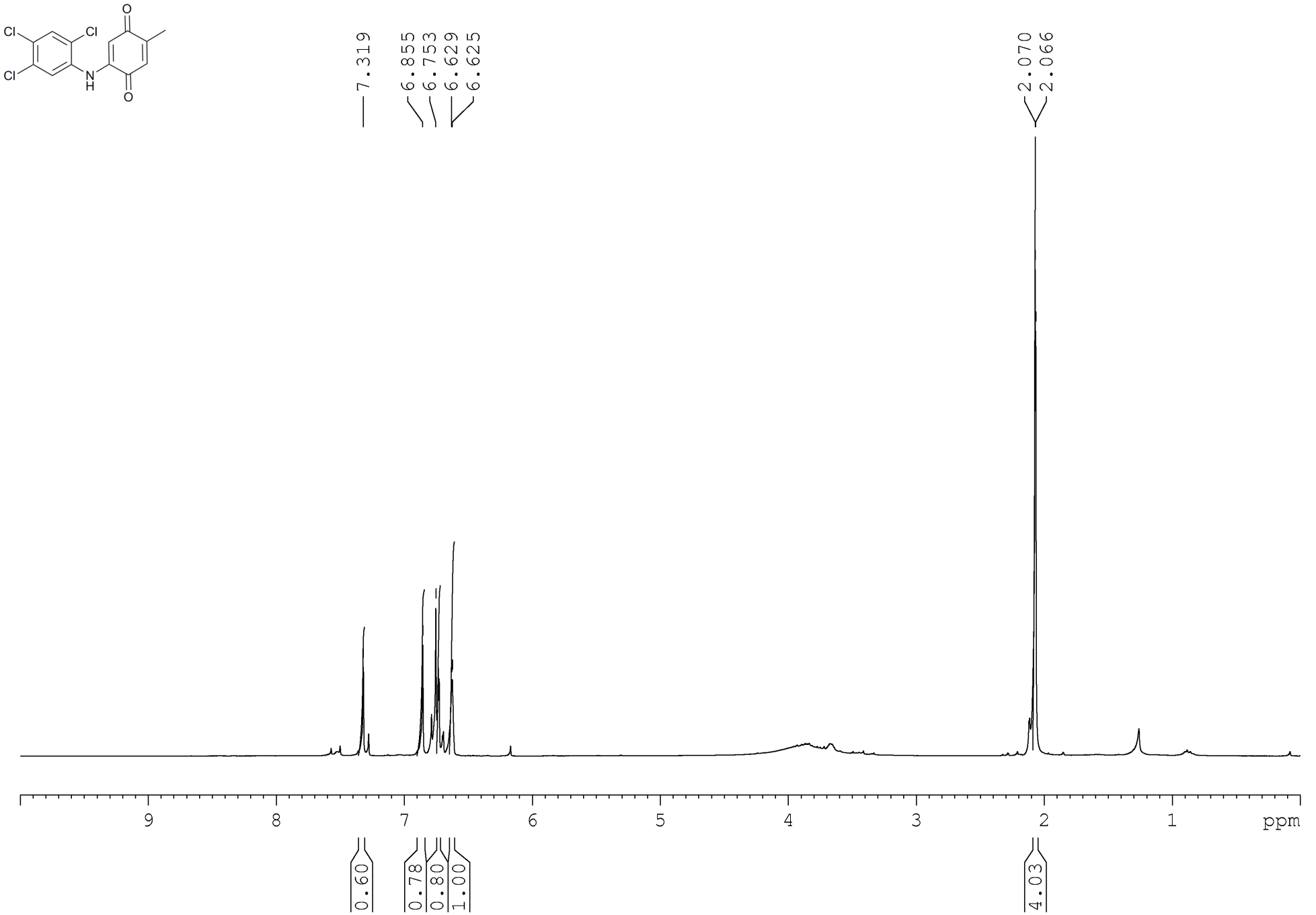

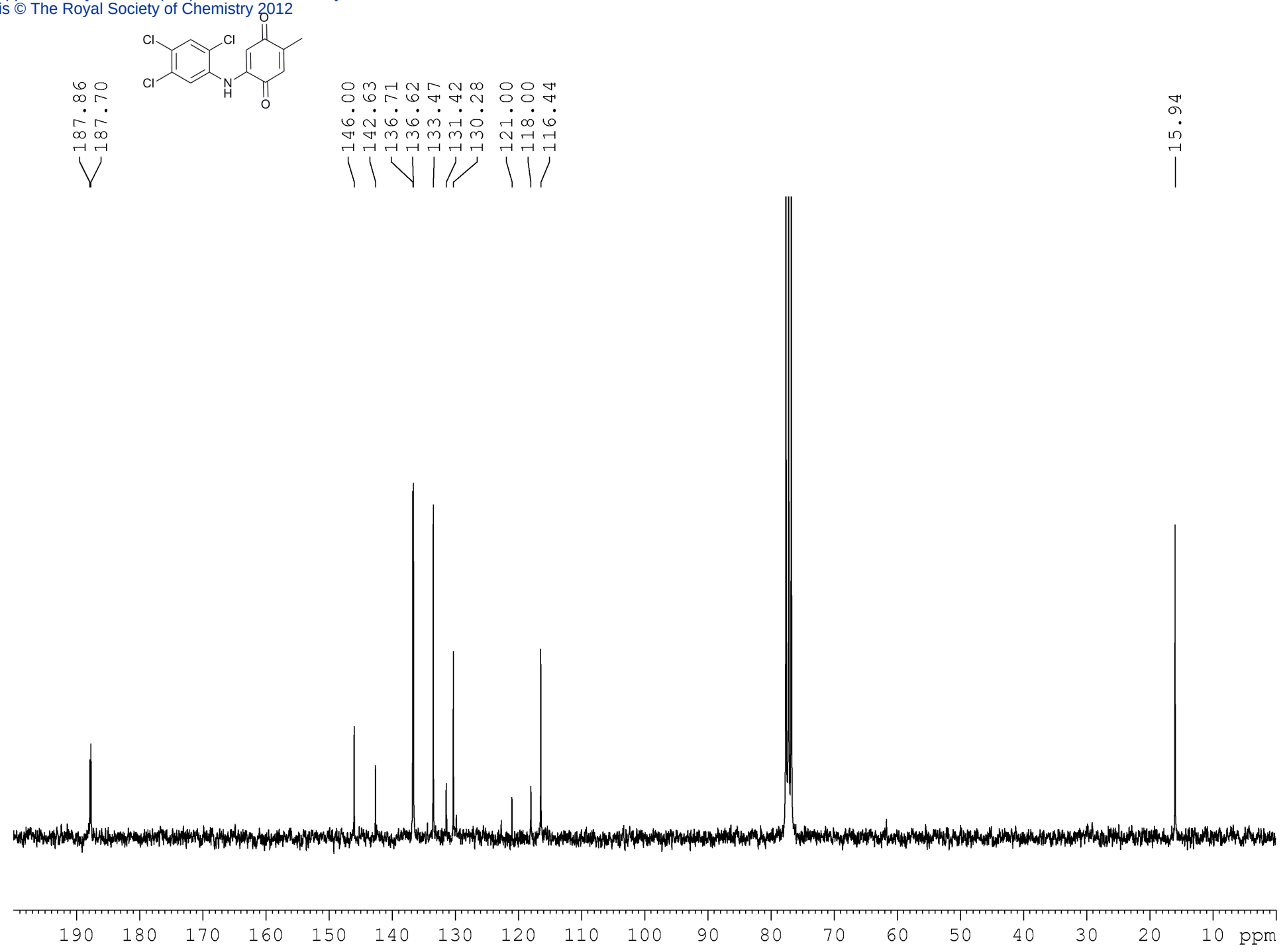

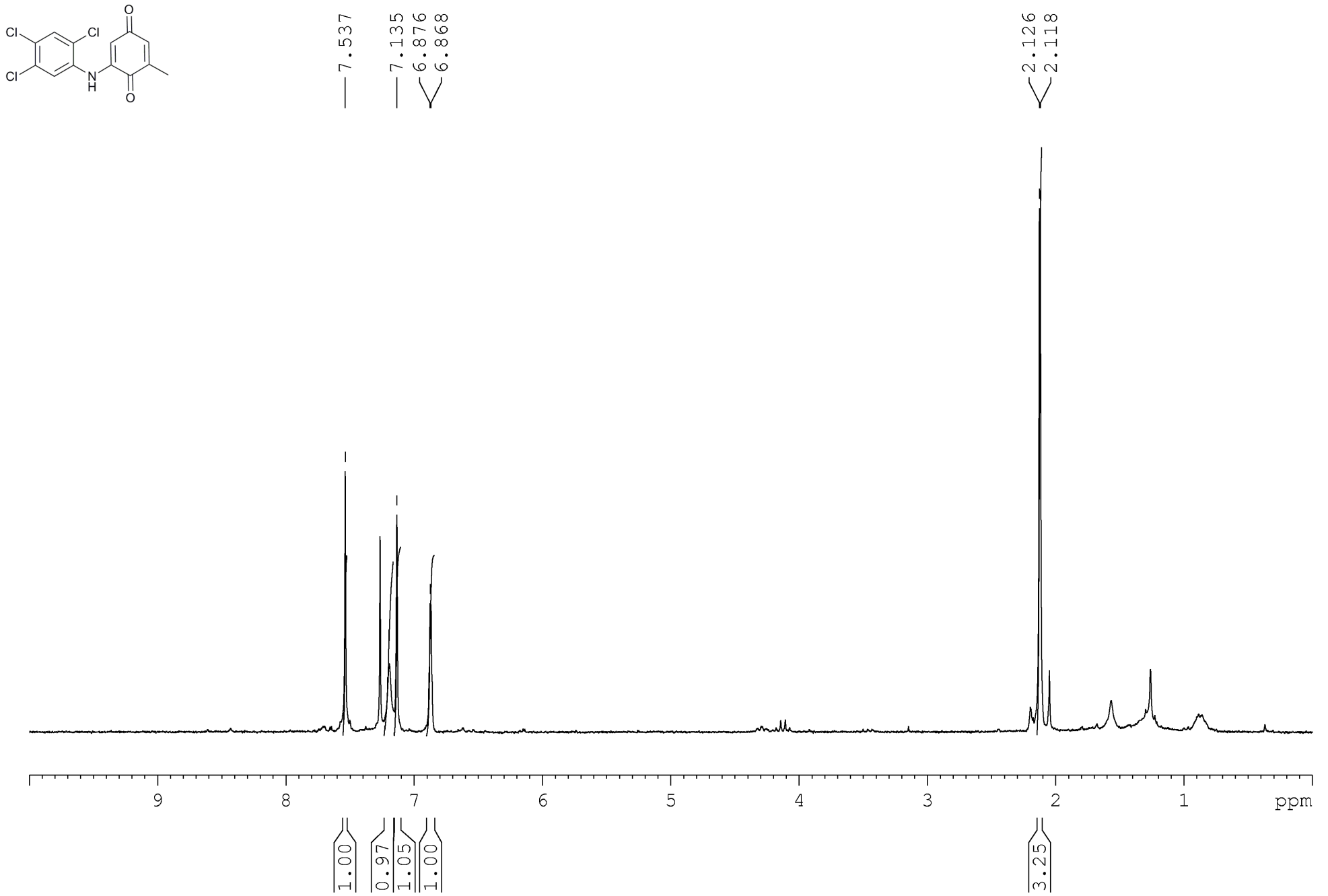

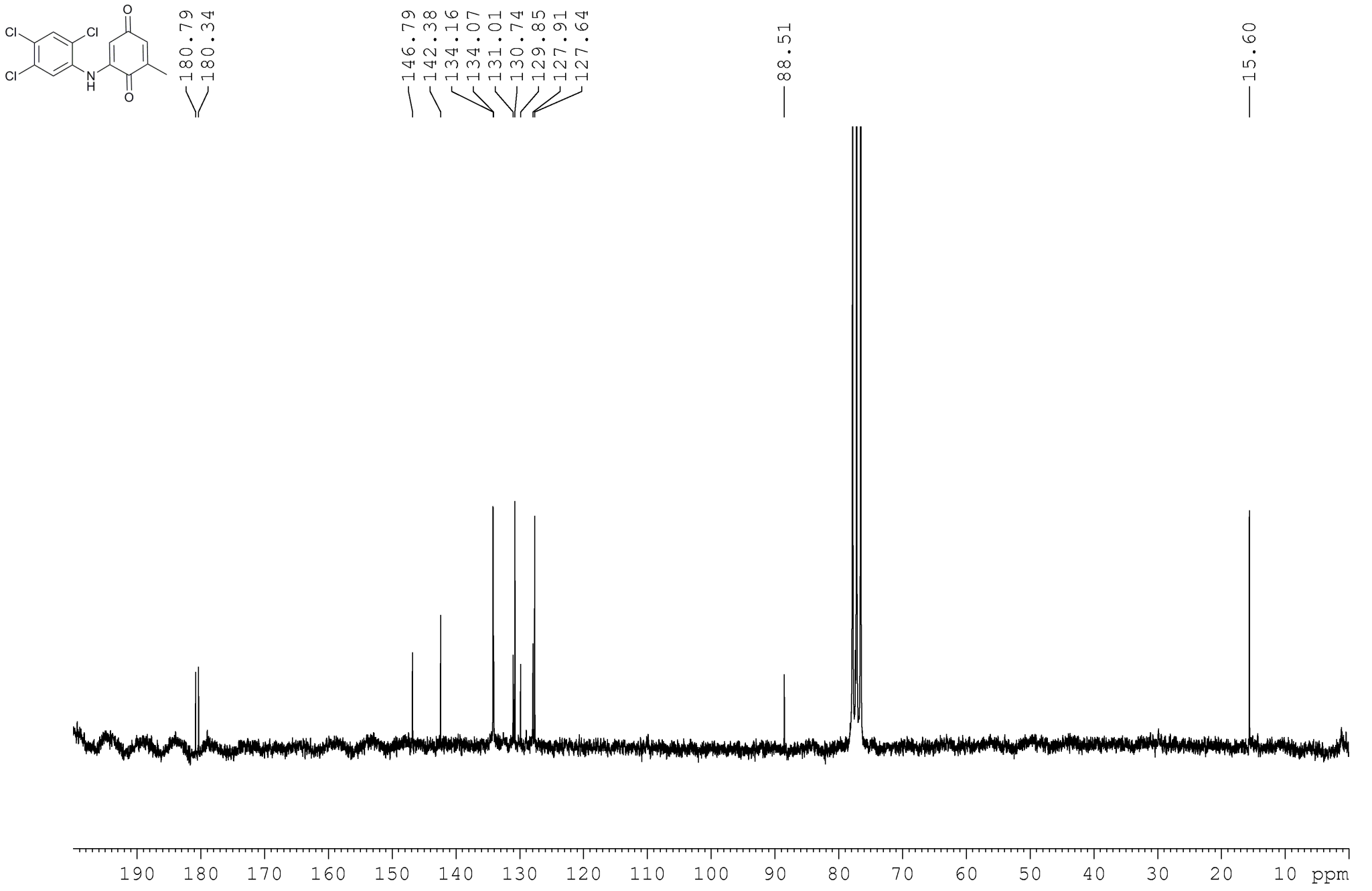

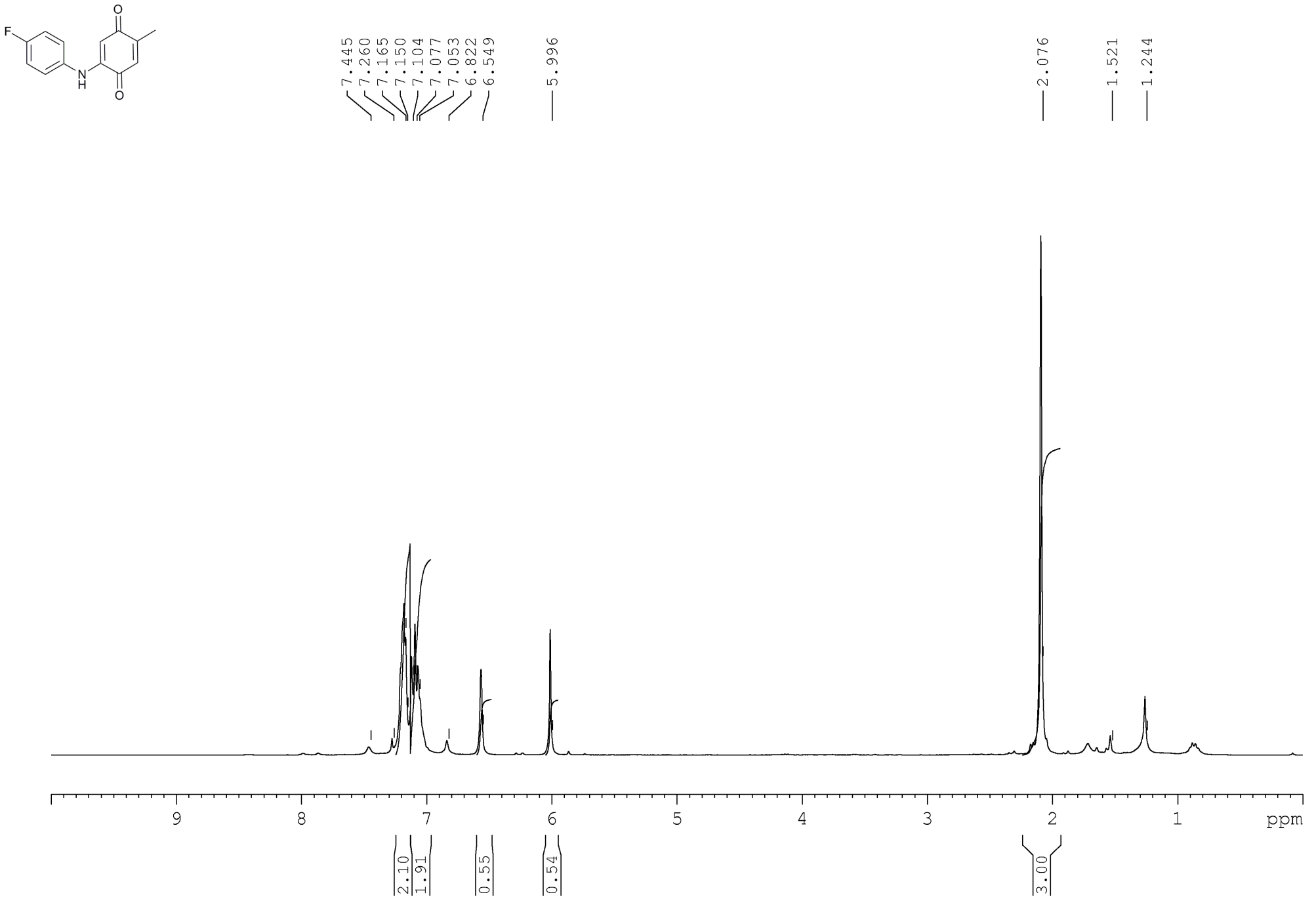

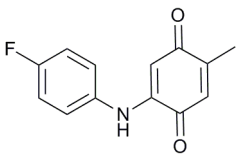

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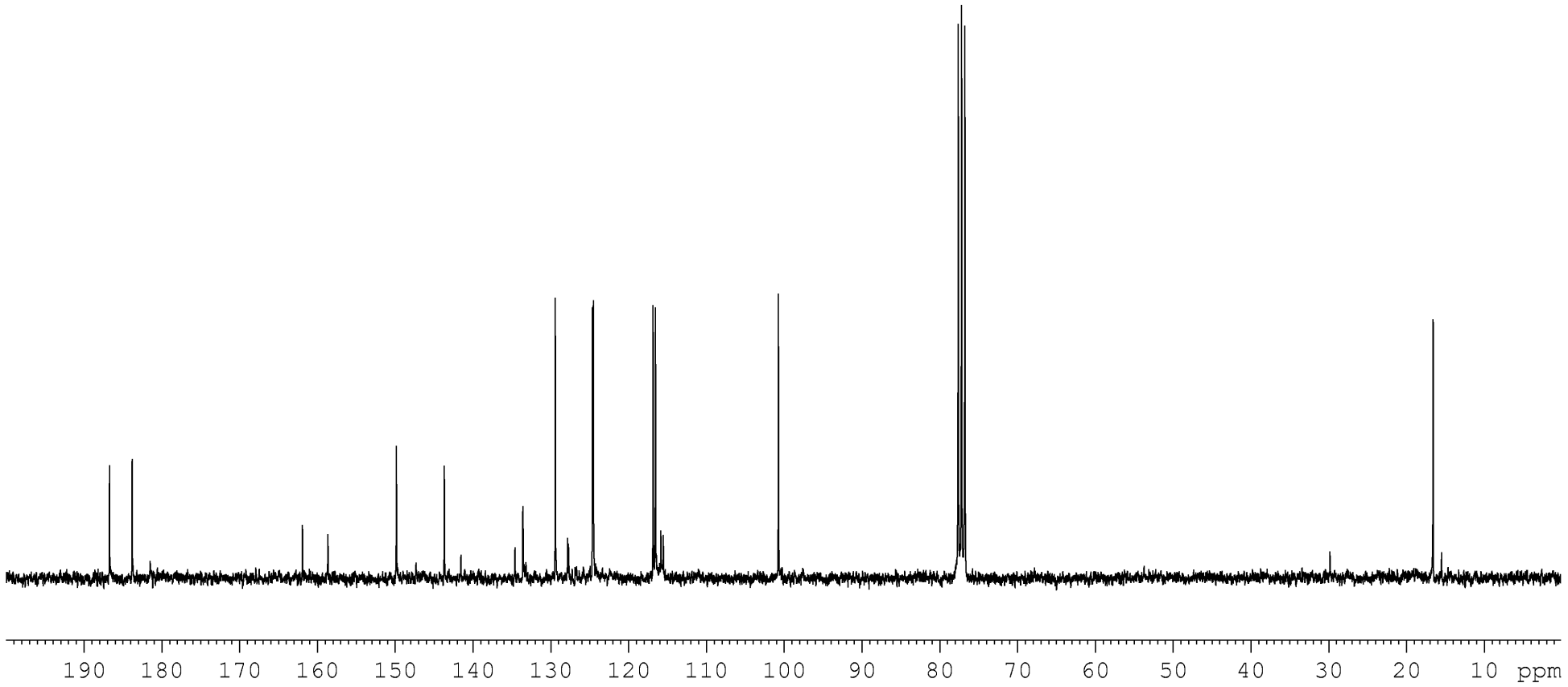

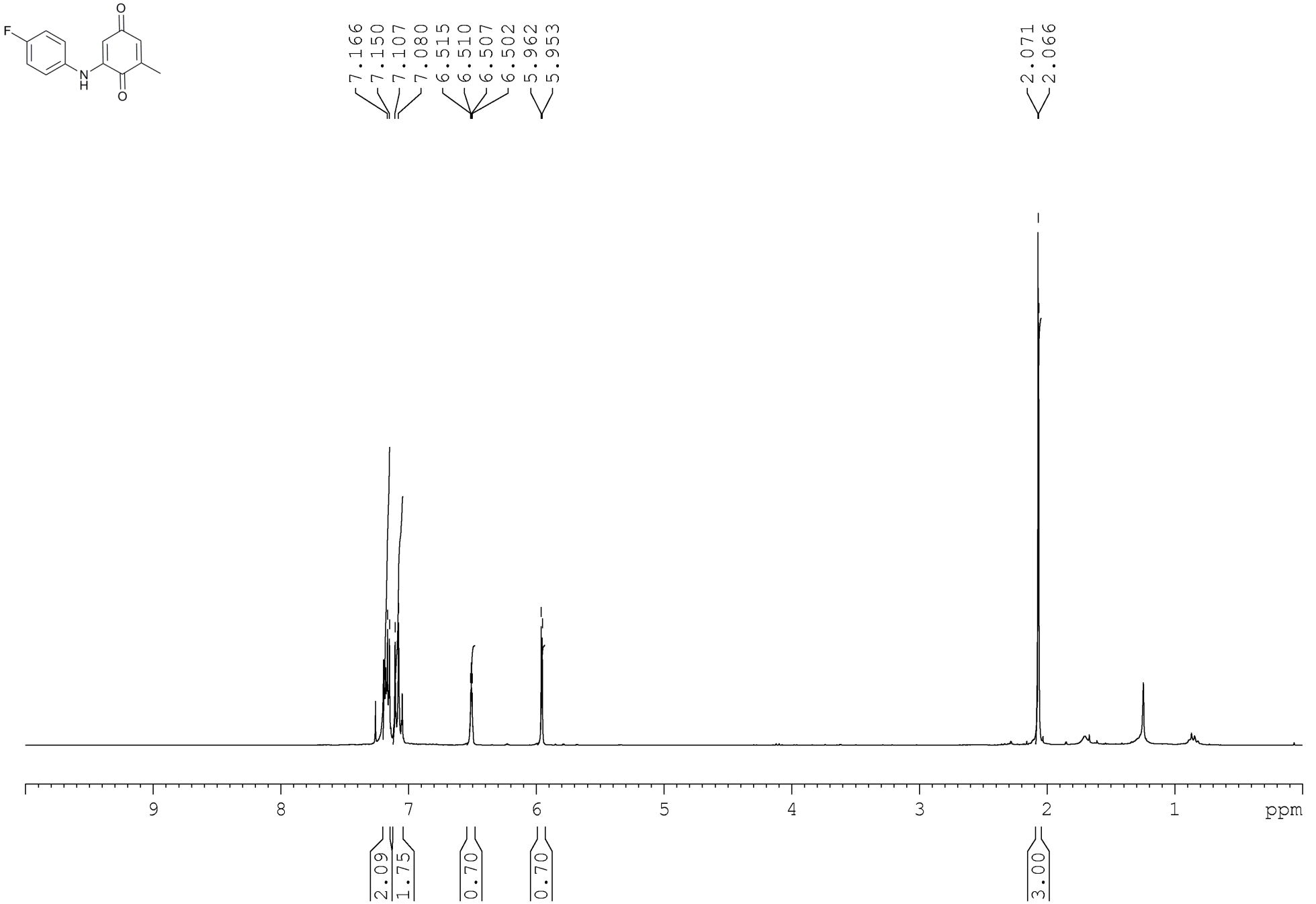

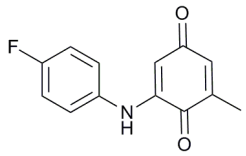

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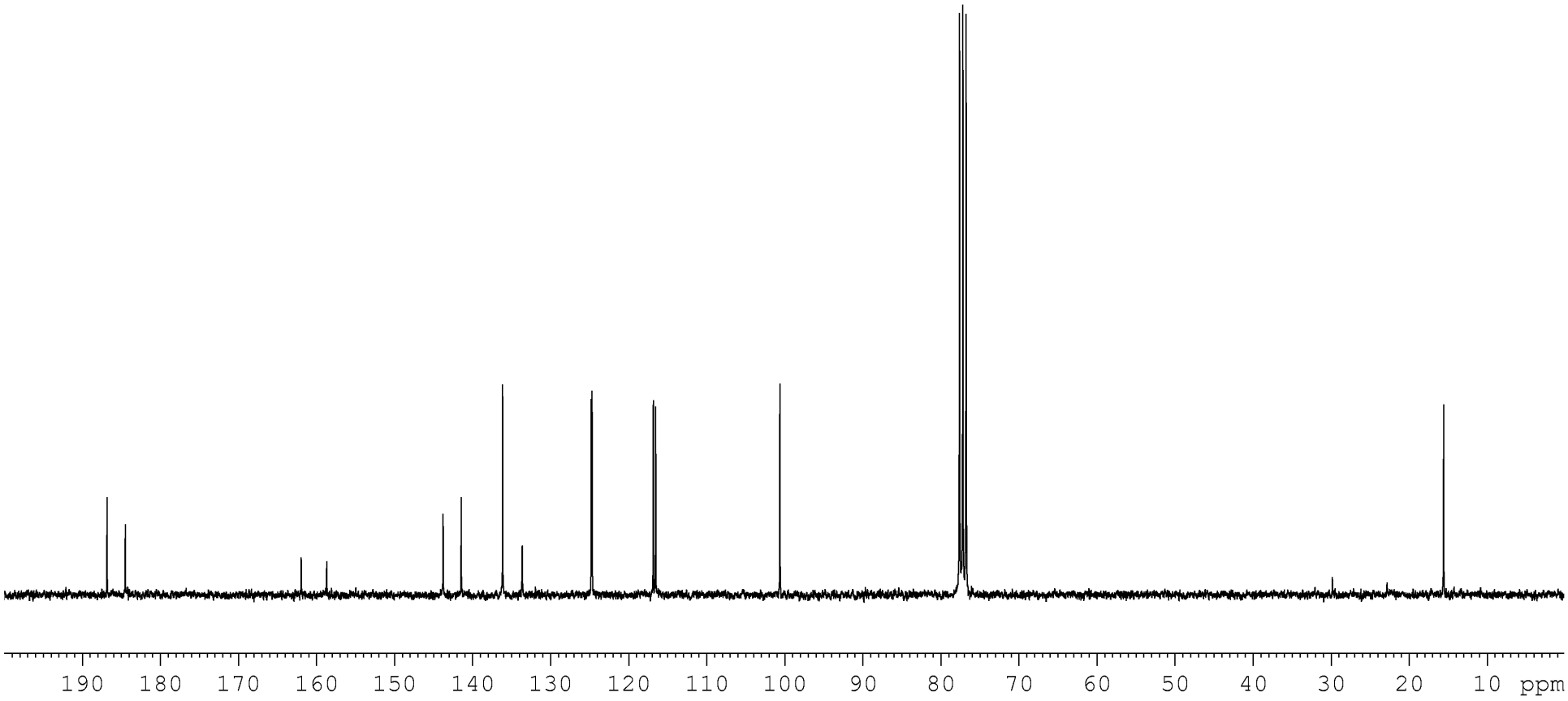

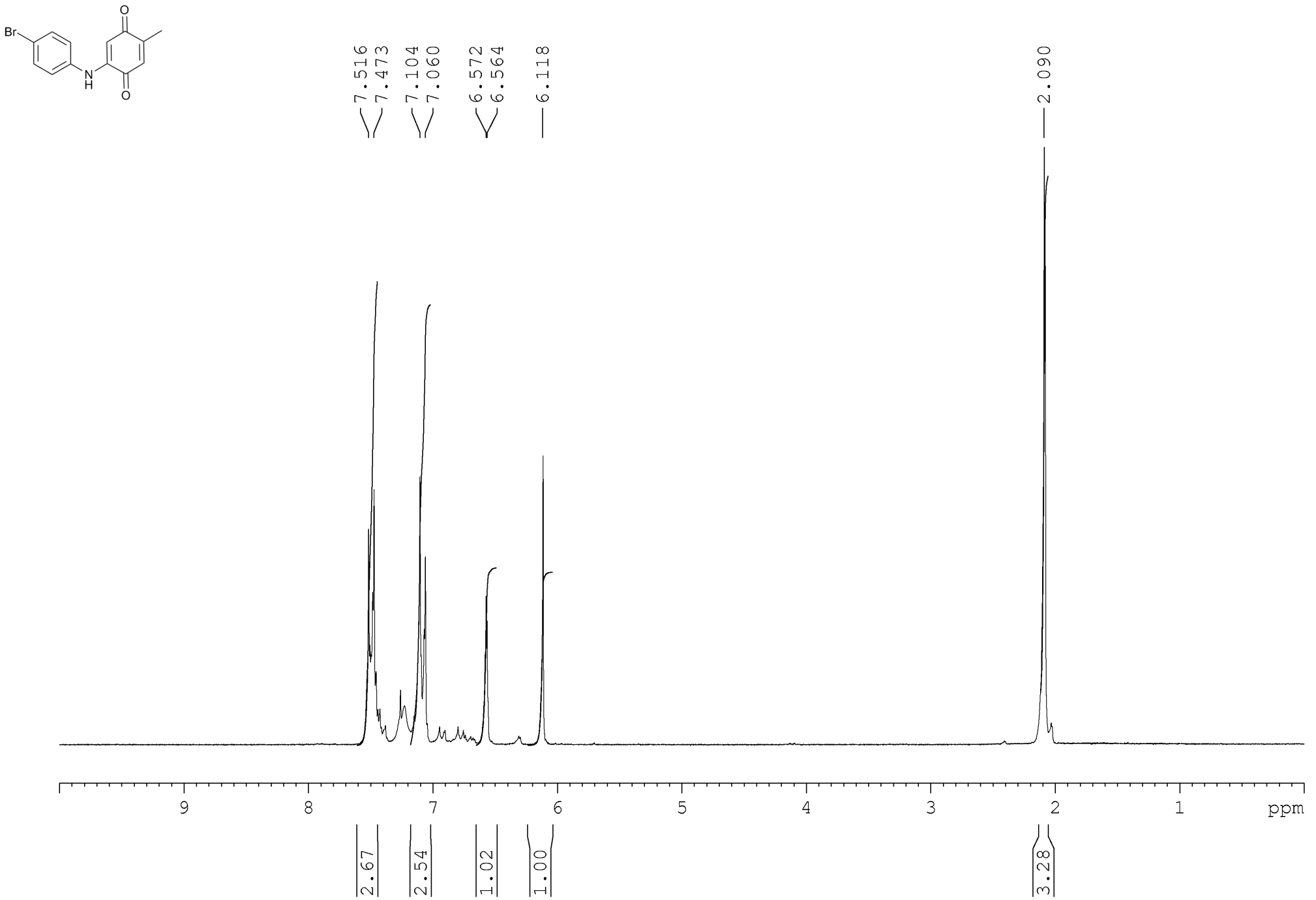

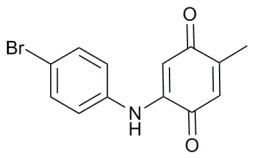

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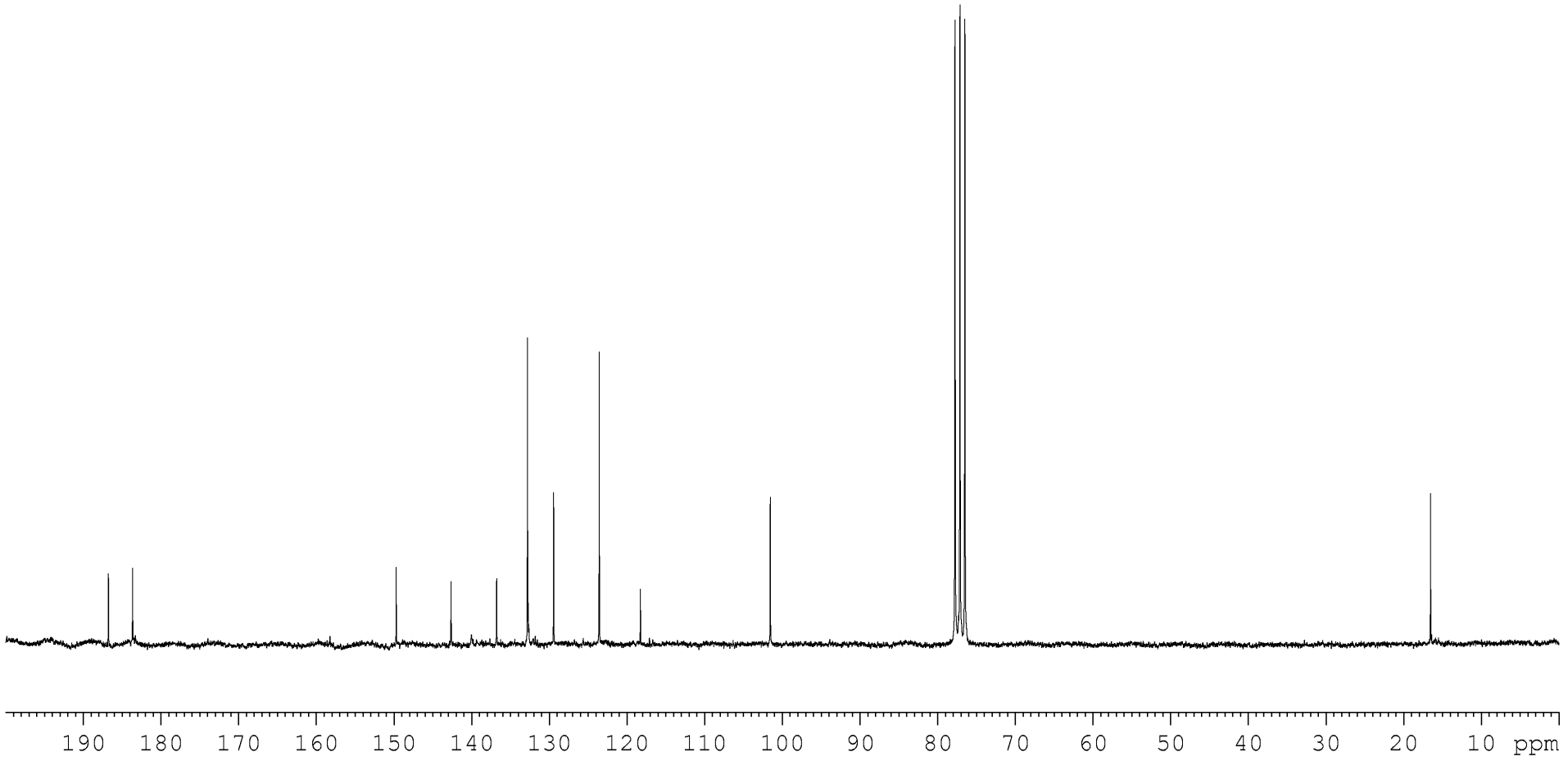

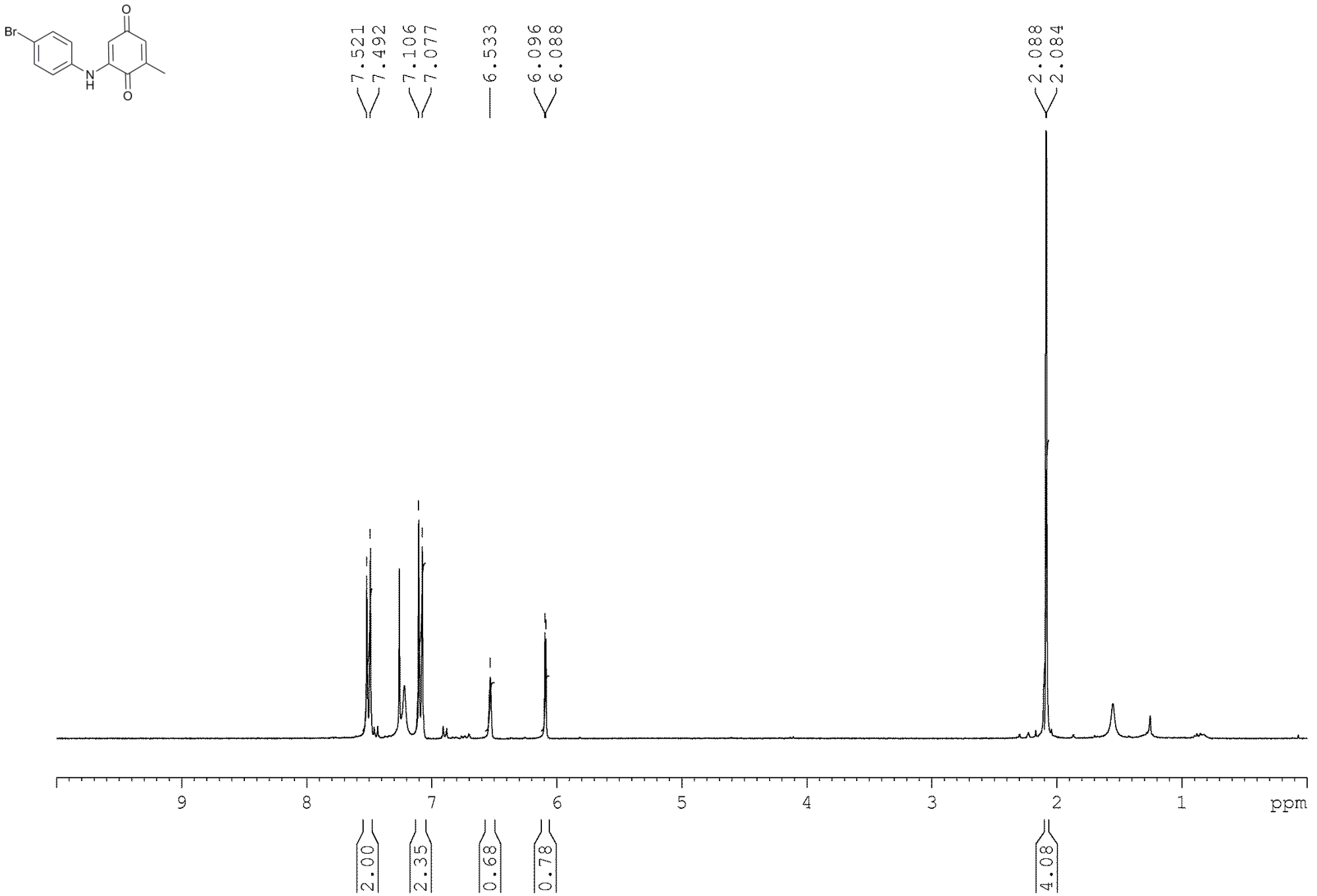

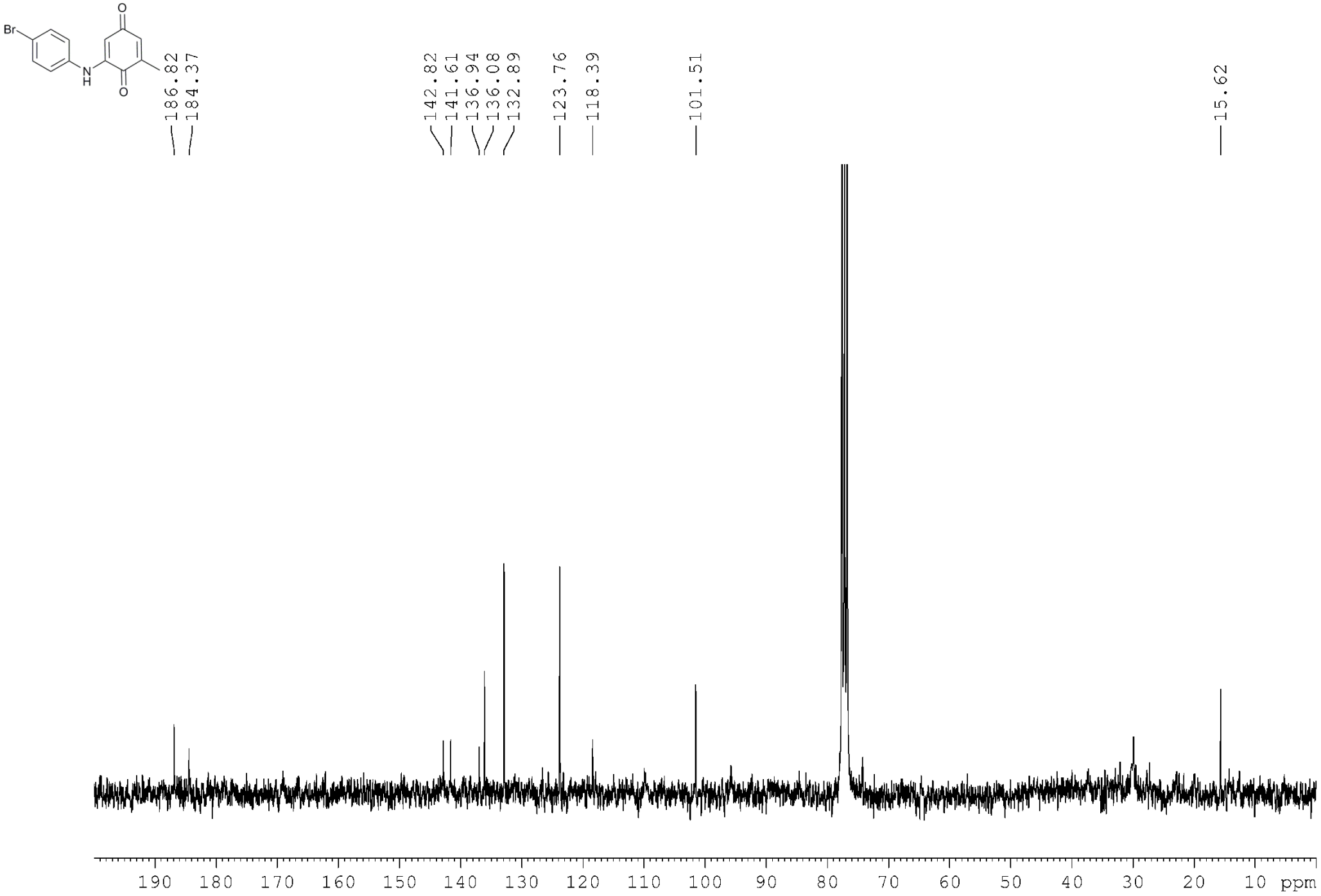

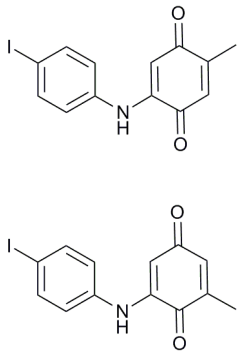

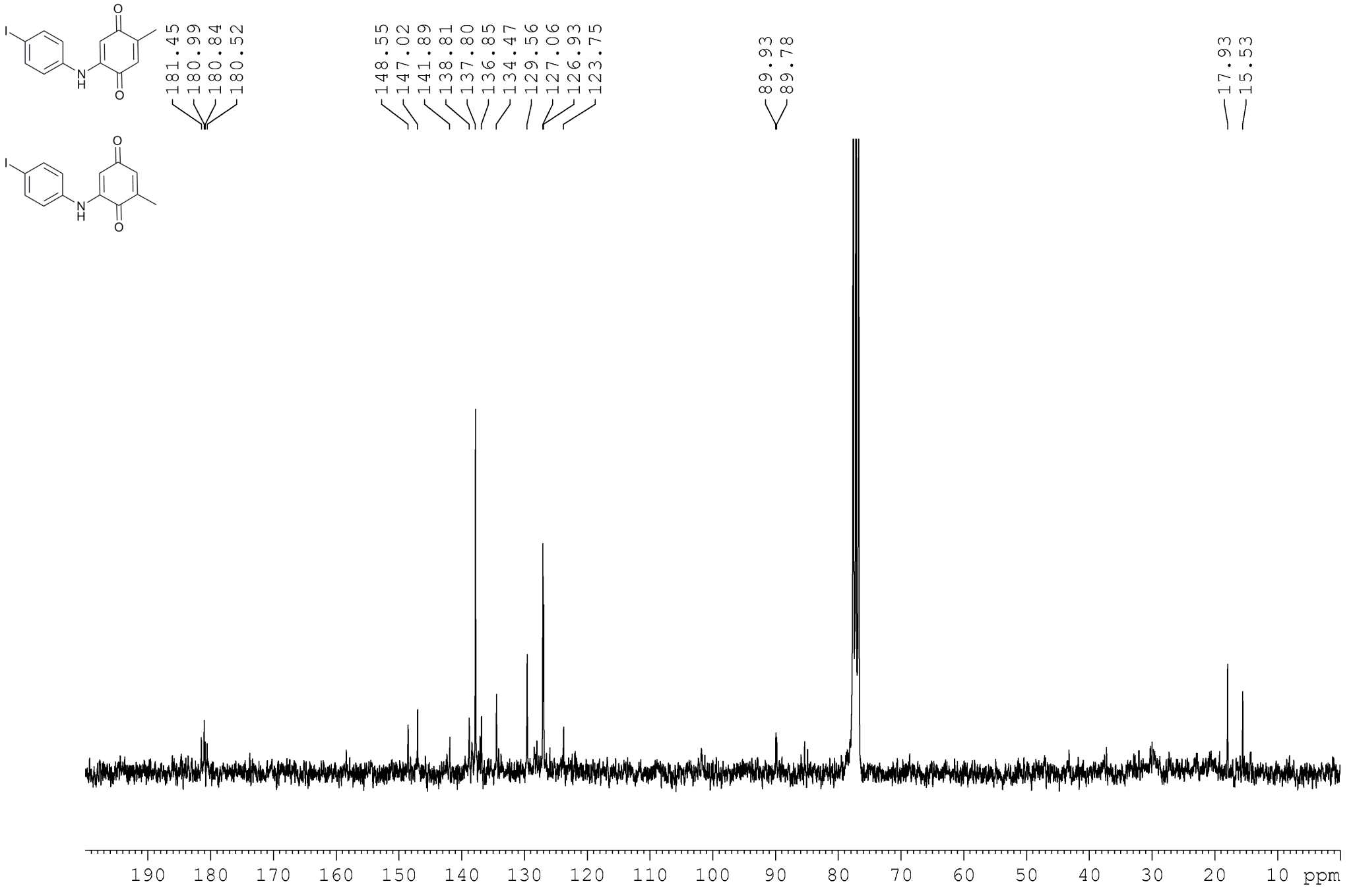

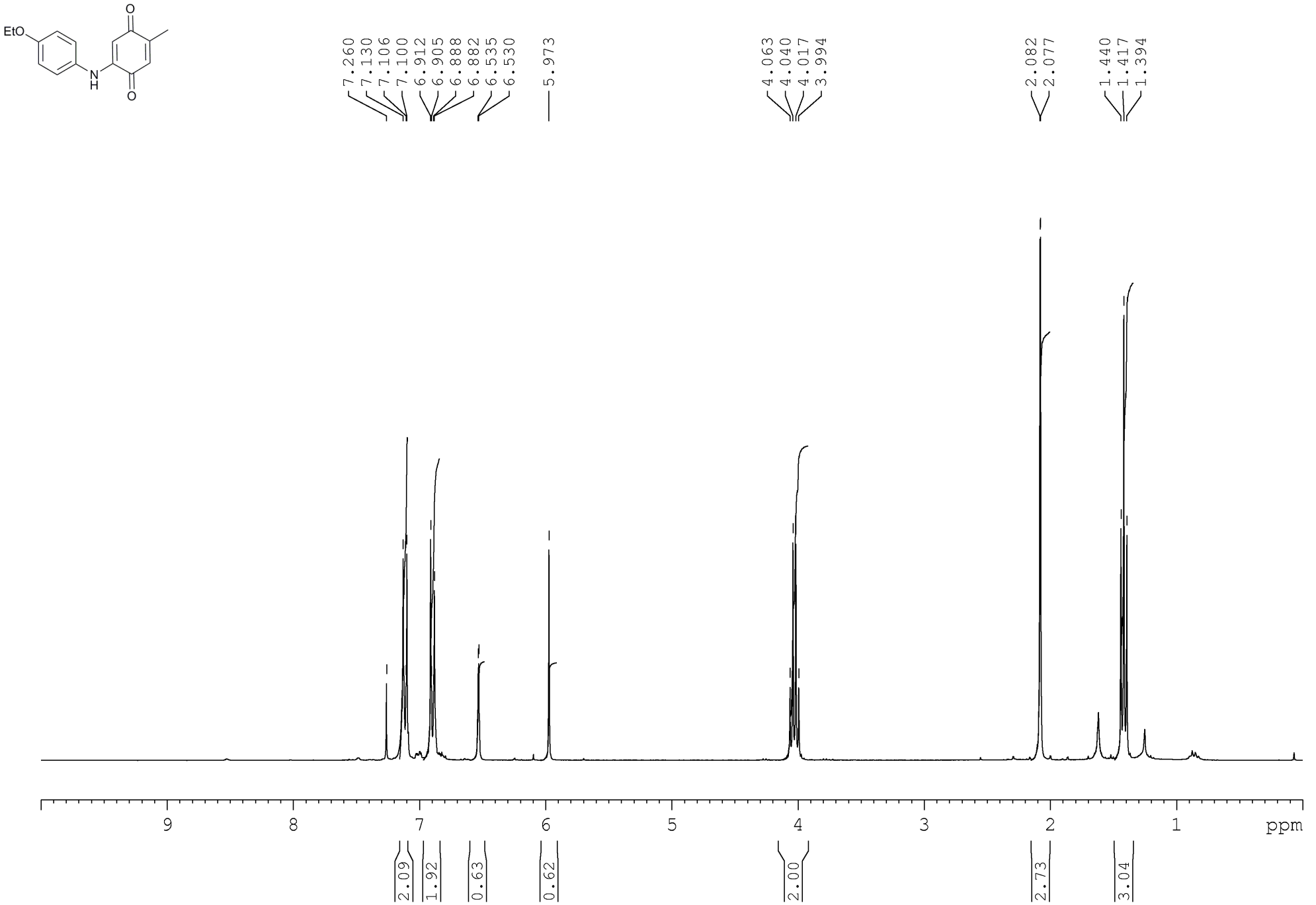

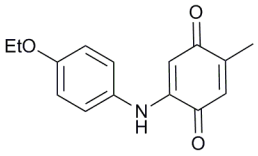

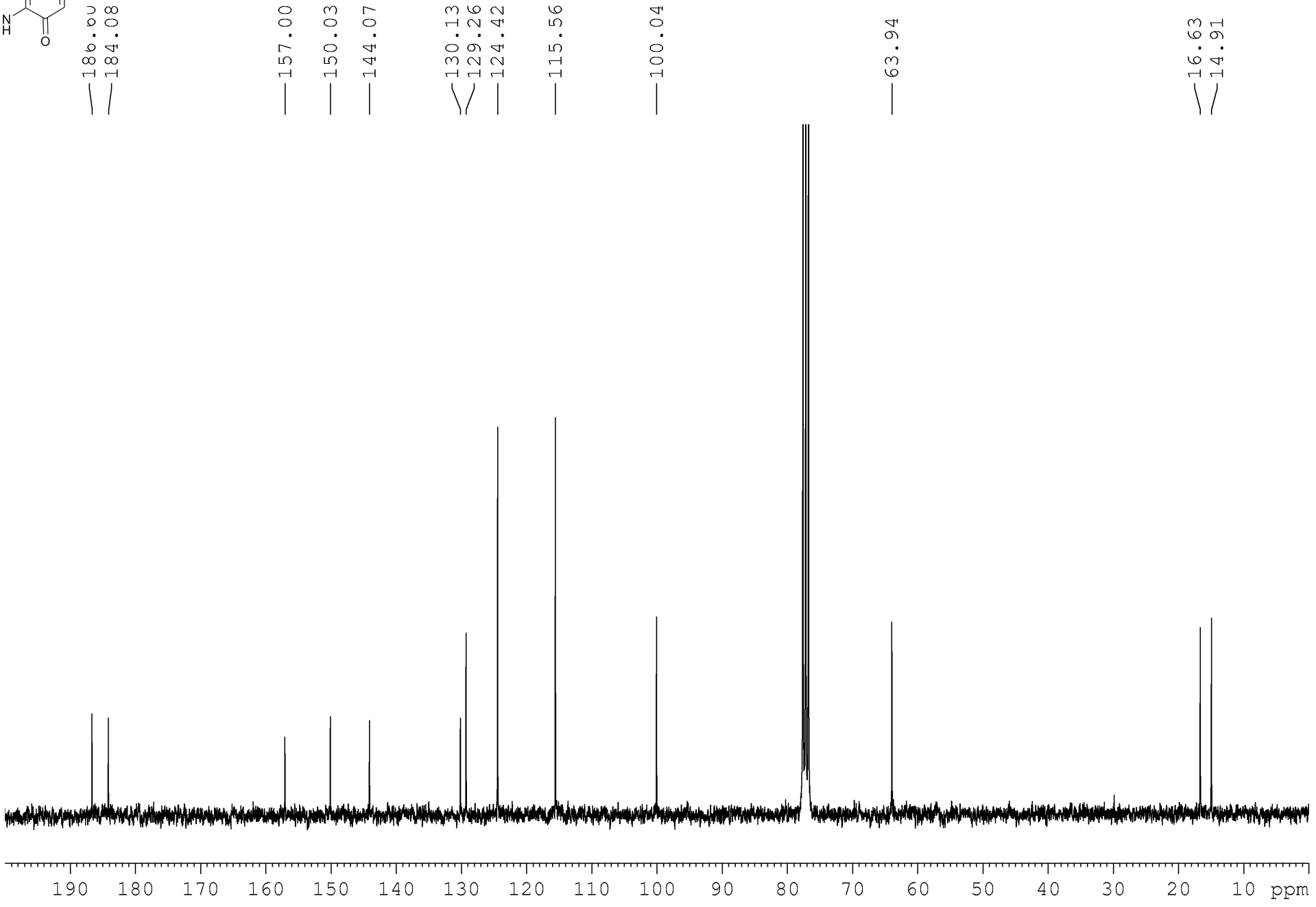

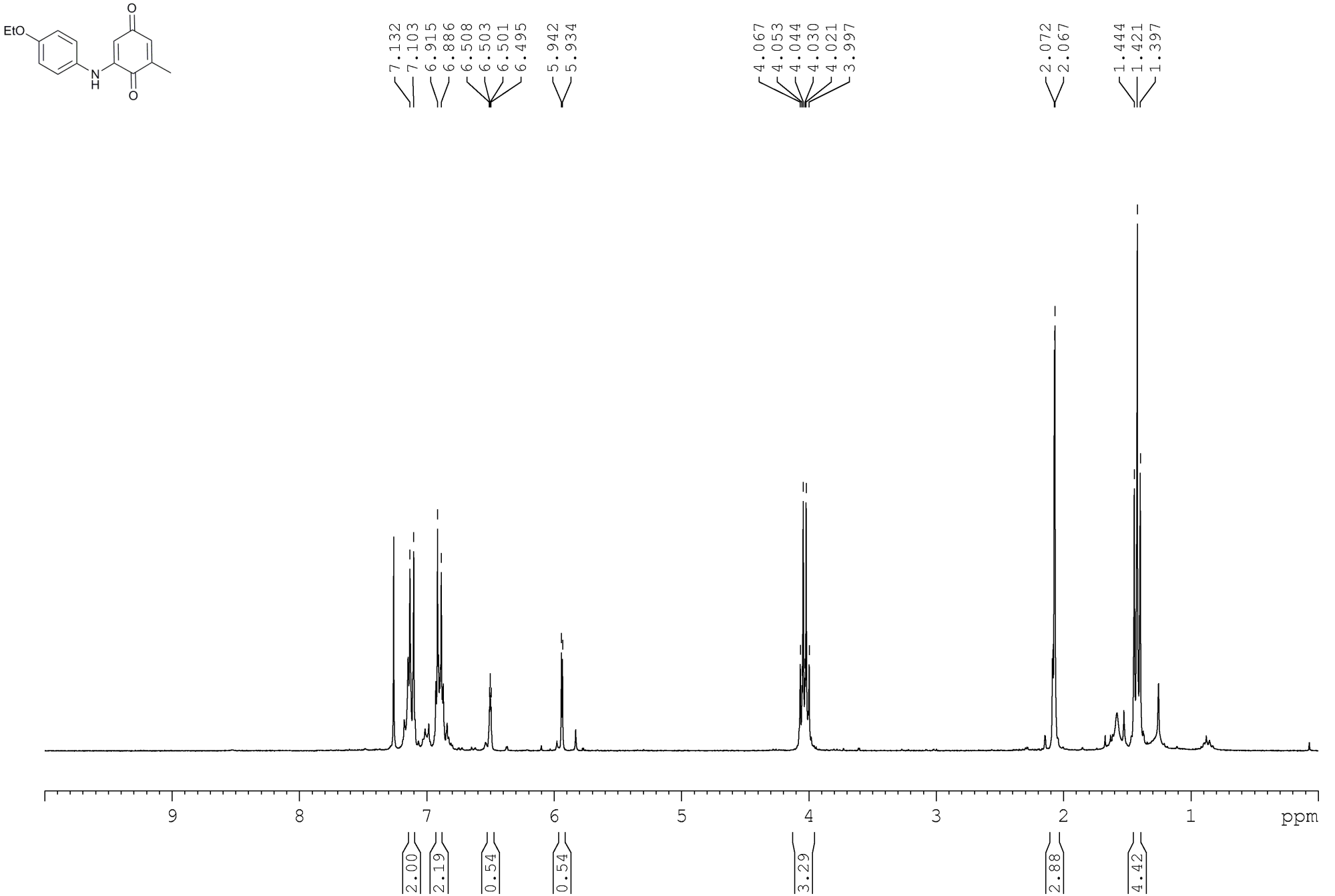

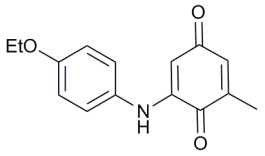

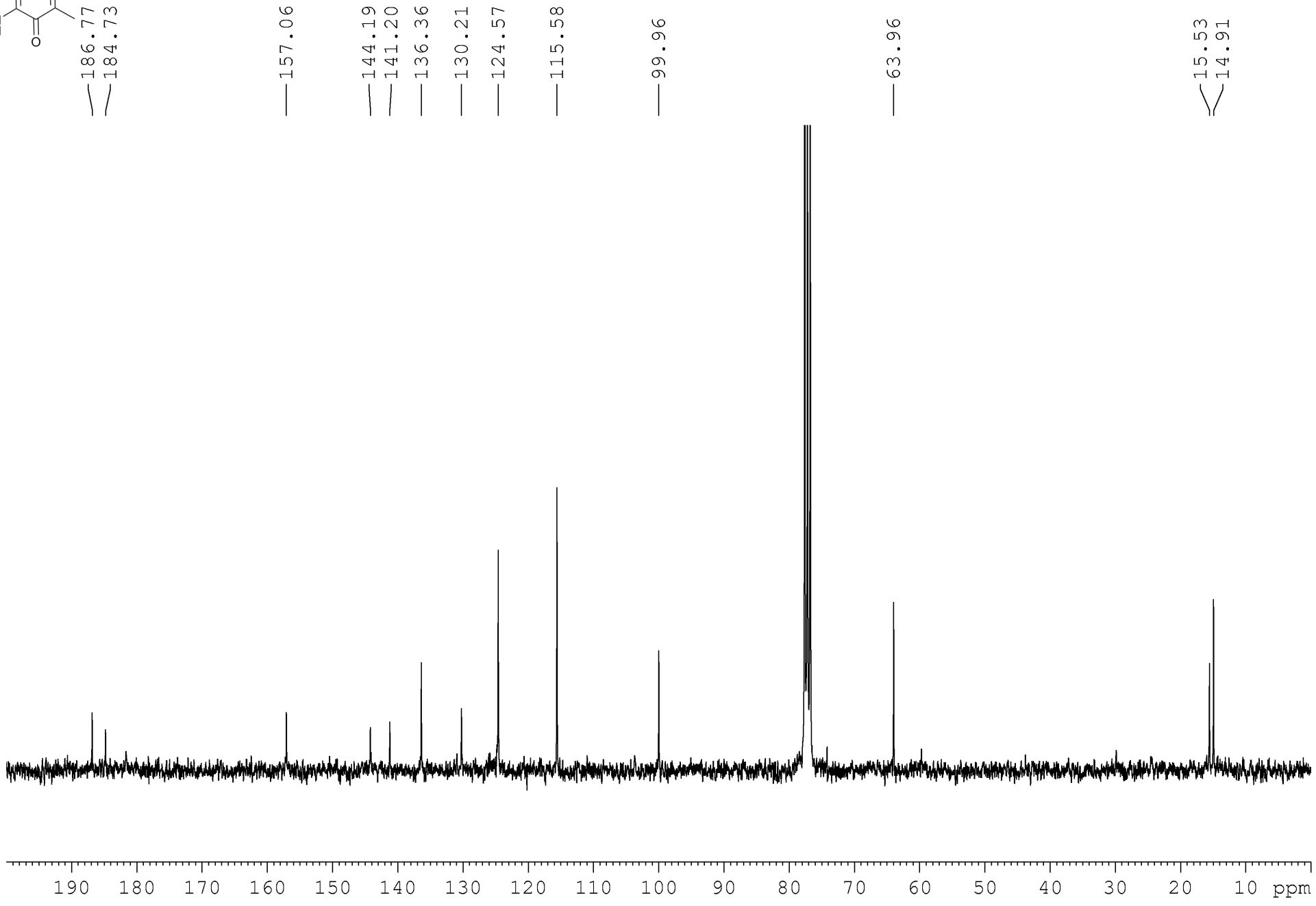

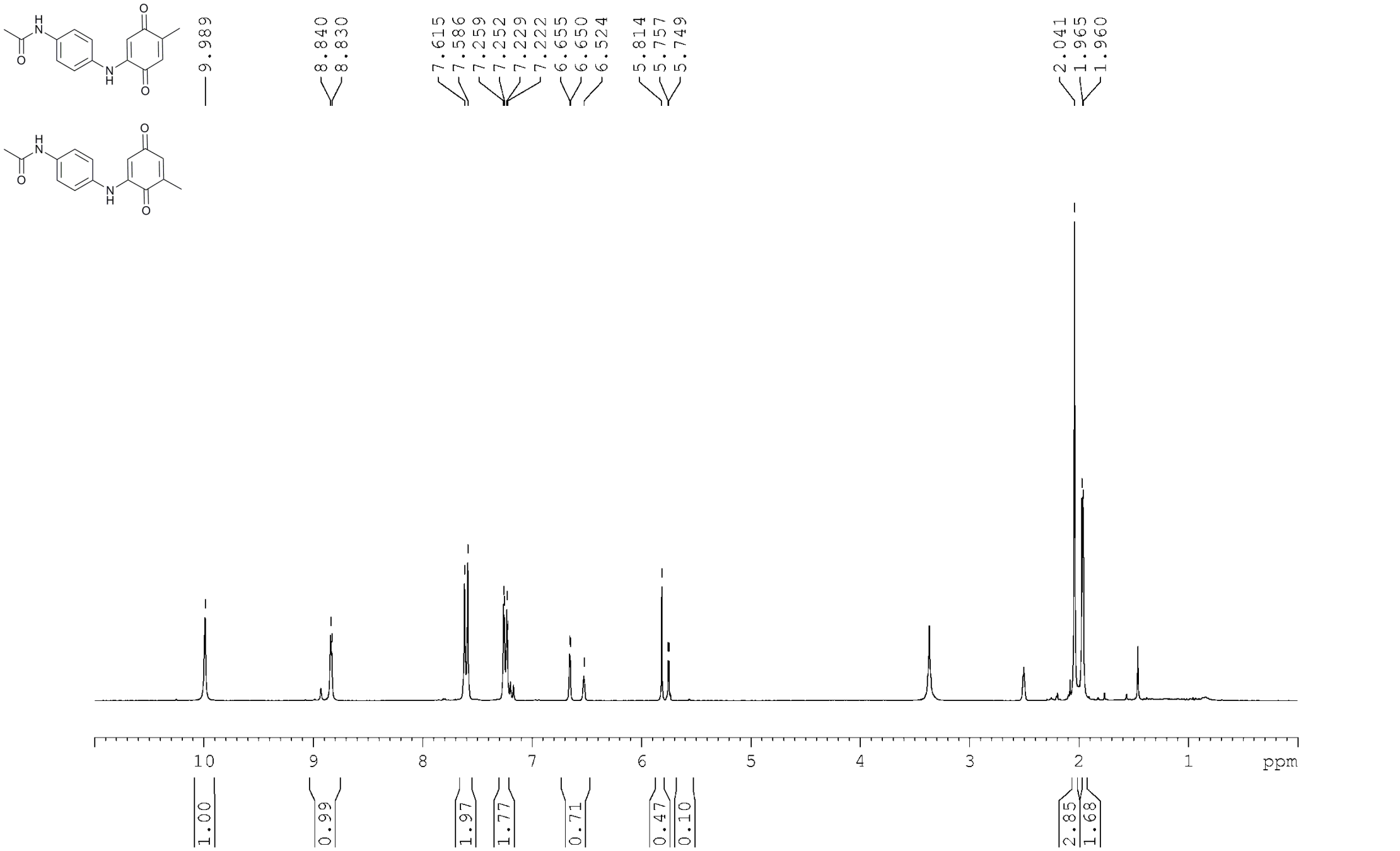

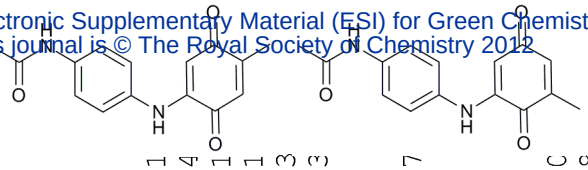

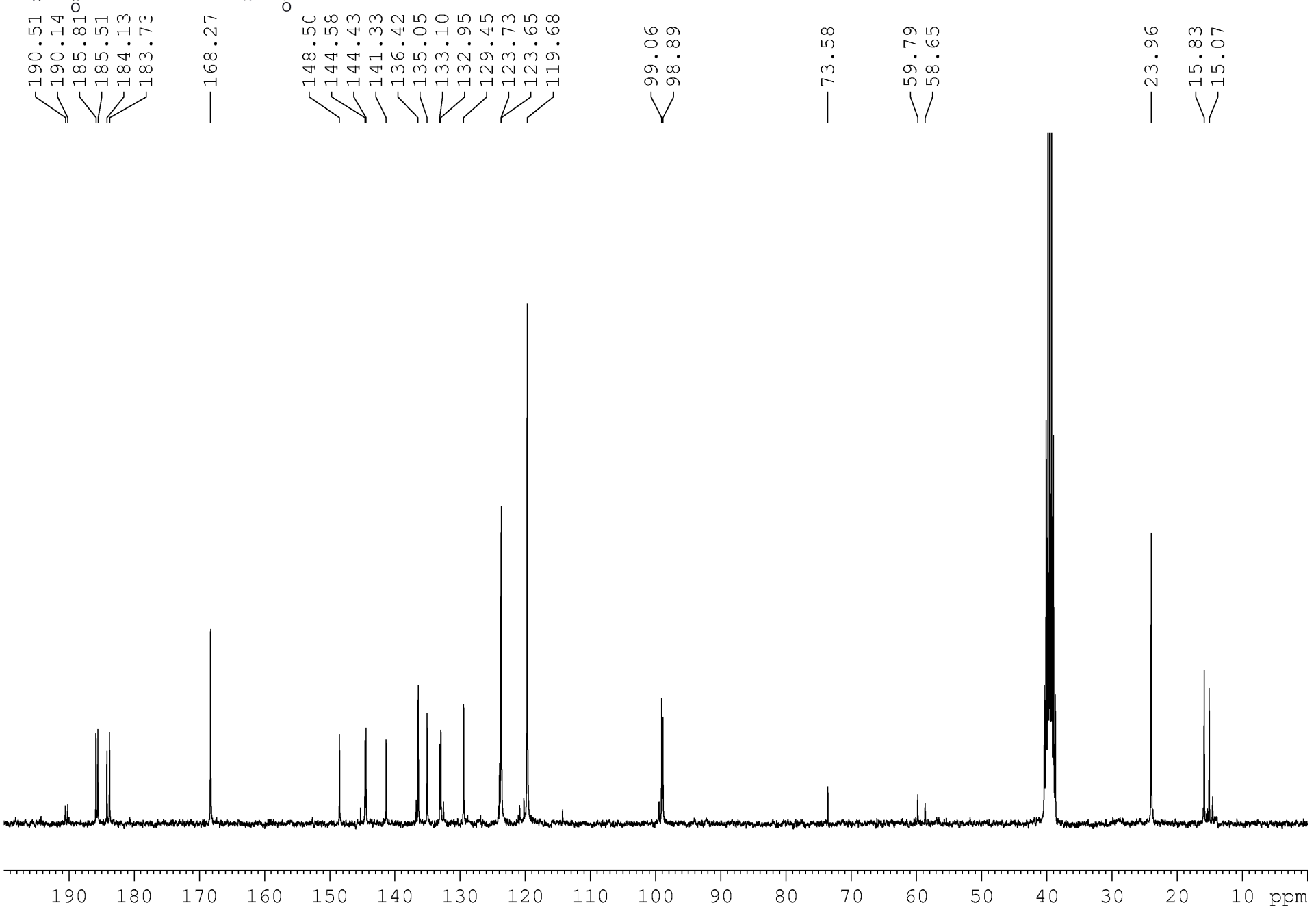

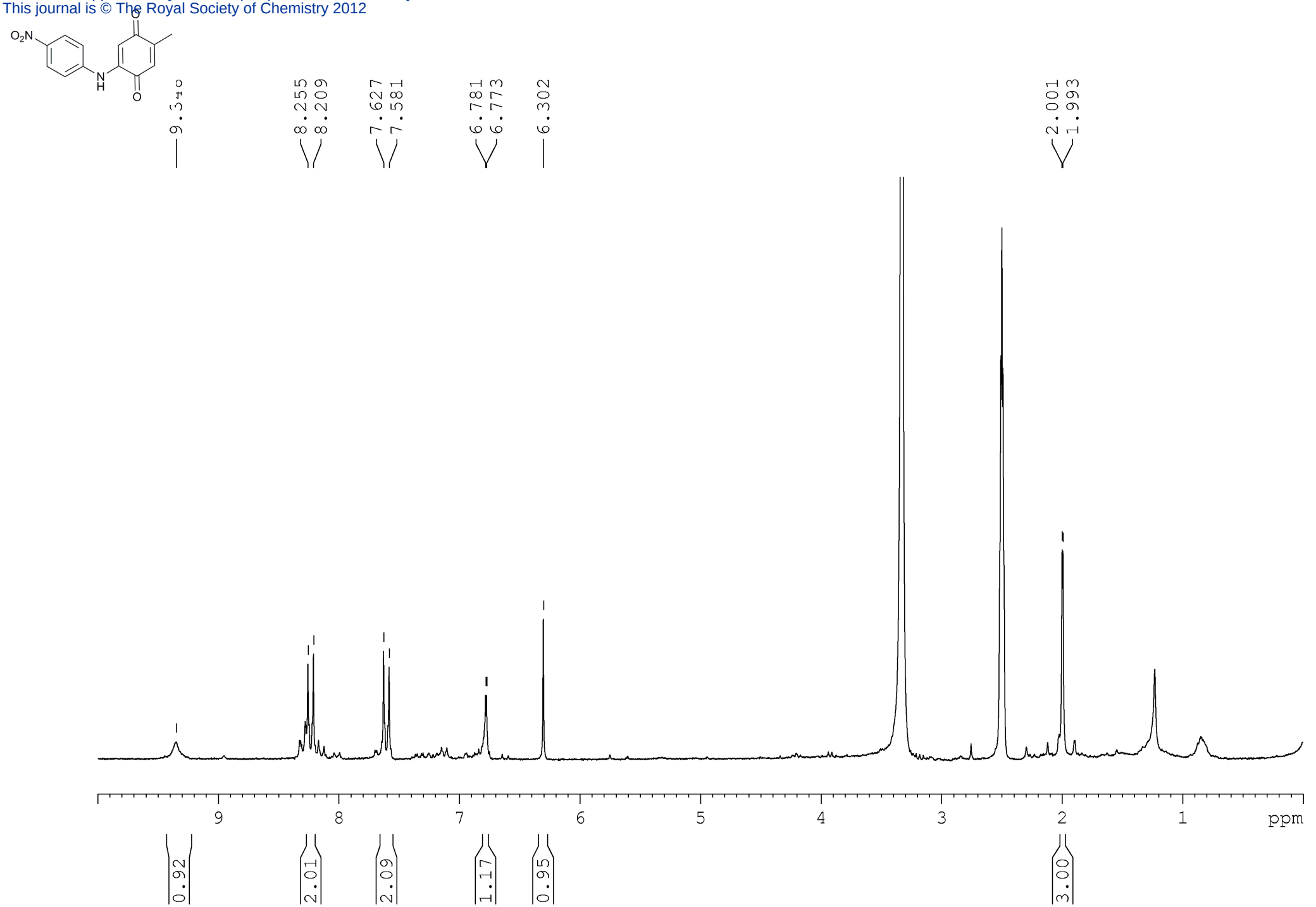

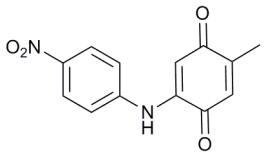

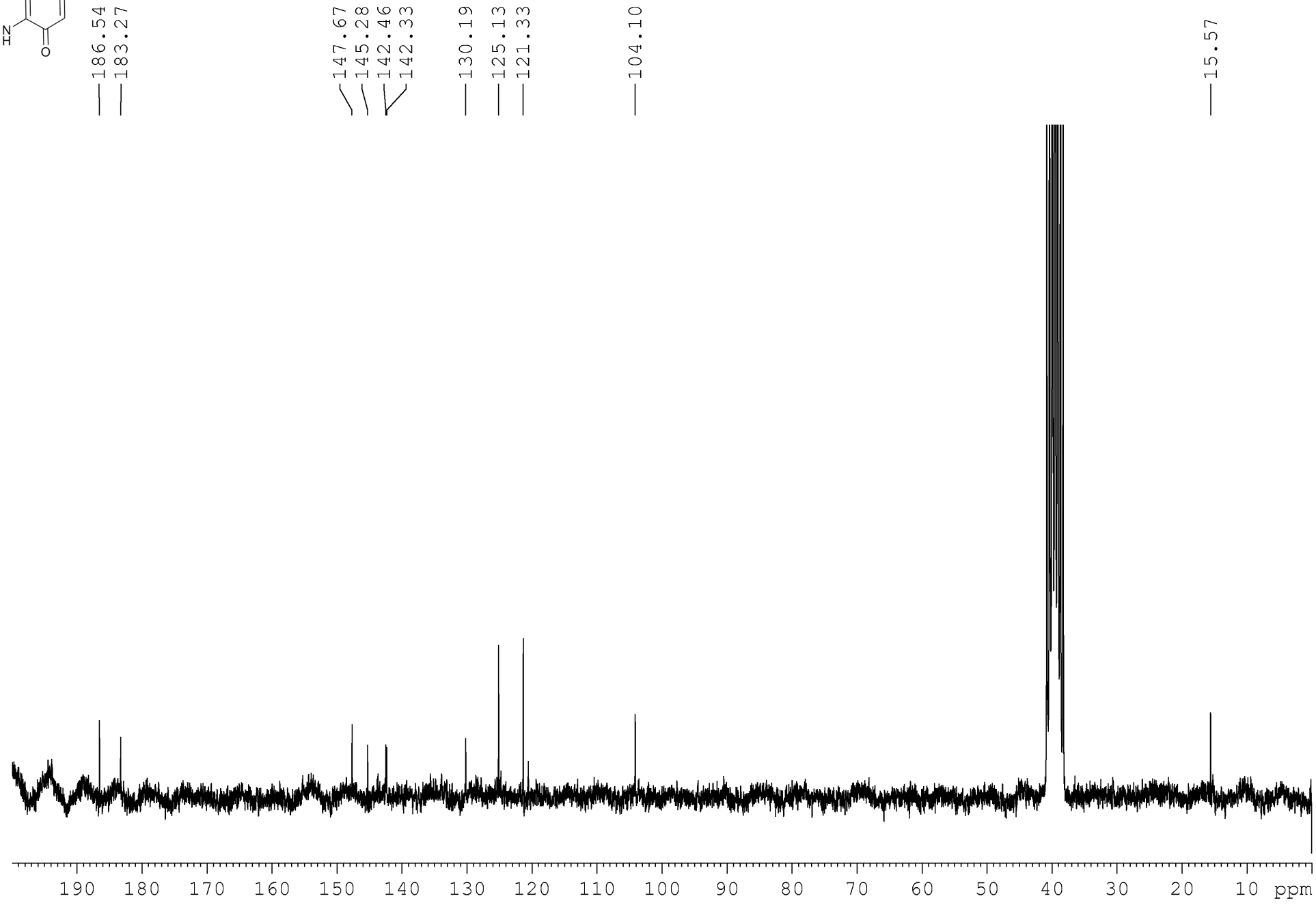

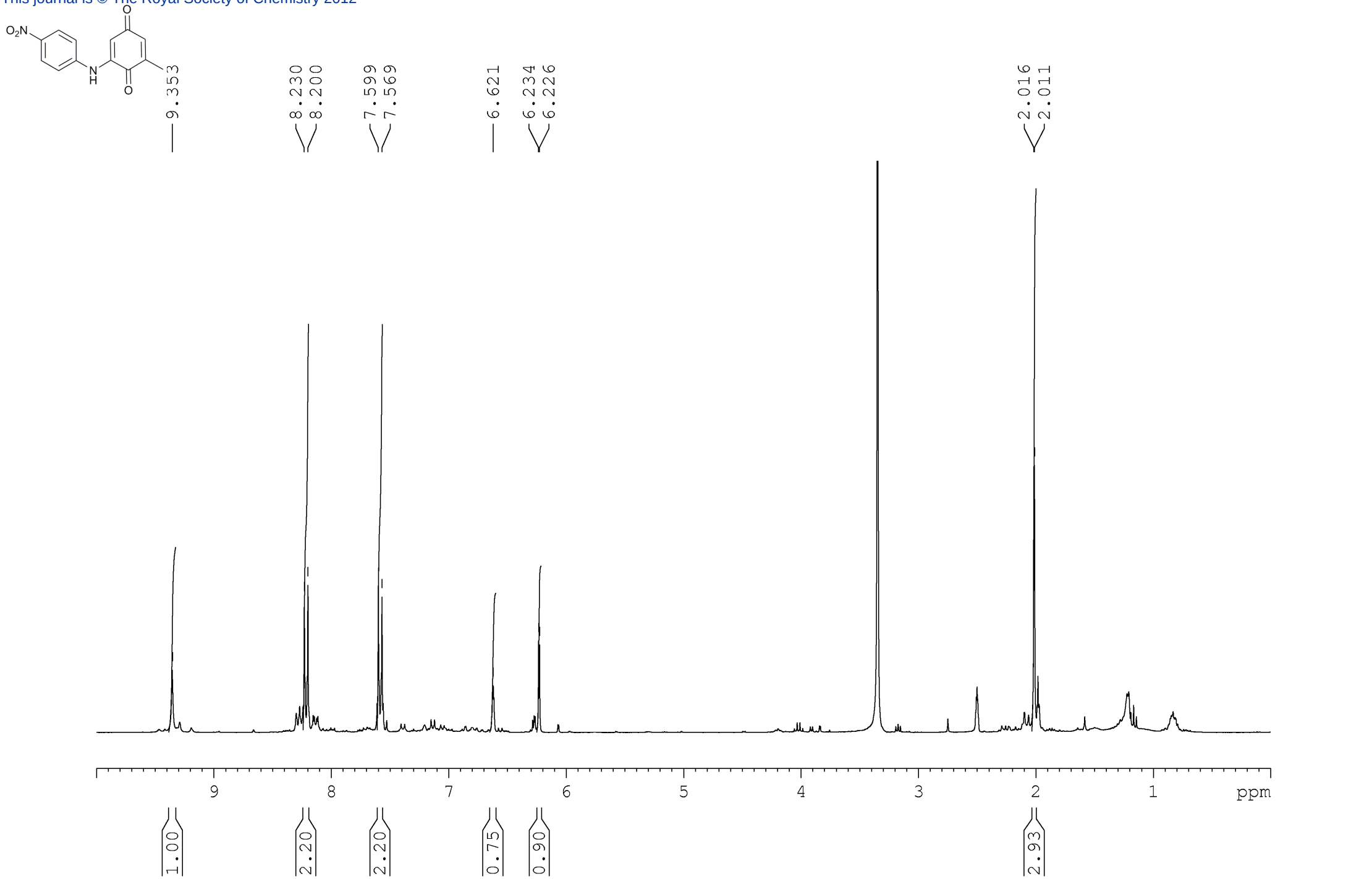

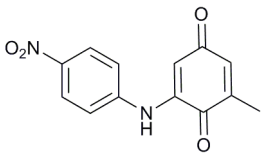

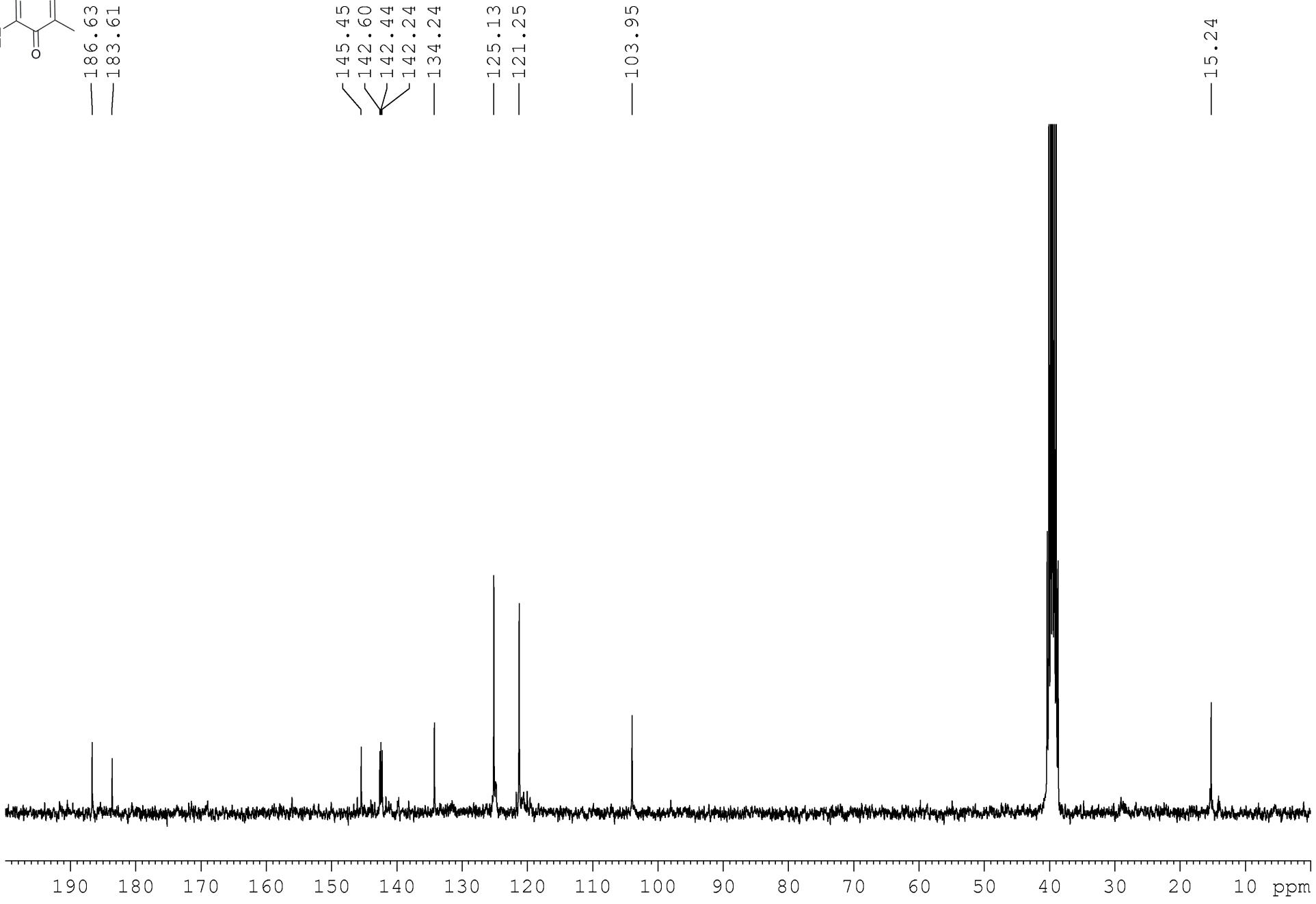

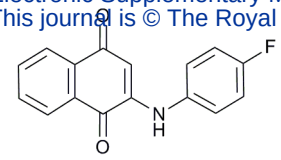

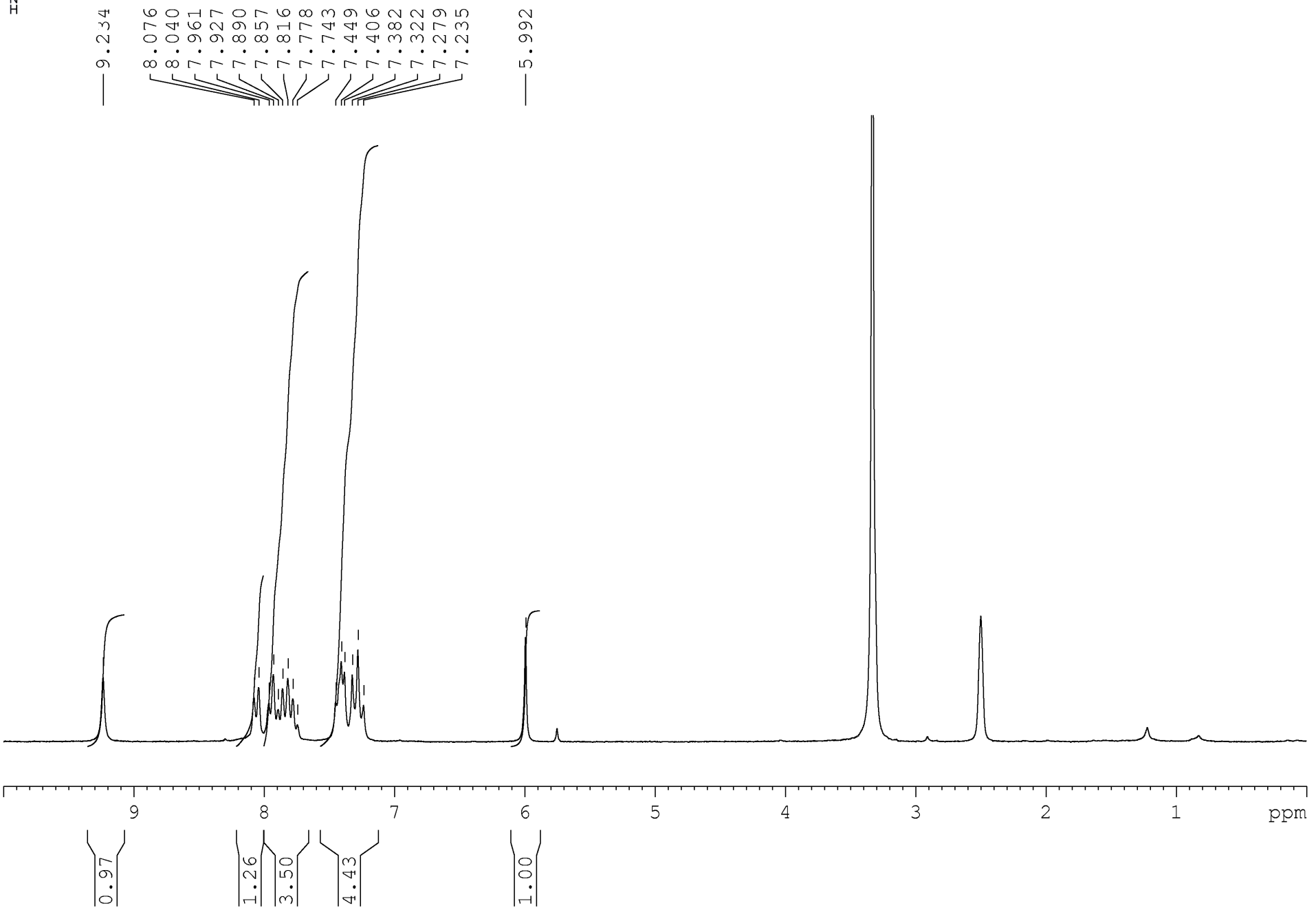

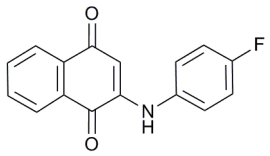

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